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A REVIEW: PHARMACOLOGY OF TRIDAX PROCUMBENS

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ABSTRACT

Tridax procumbens is a plant used majorly in Indian traditional medicine. This is rich in alkaloids, steroids, carotenoids, flavonoids (such as catechins, centaurein and bergenins), fatty acids, phytosterols, tannins and minerals. Concoctions of extracts from T. procumbens leaves, stem,flower, and roots are used to treat patients suffering from diabetes, arthritis, inflammatory reactions and even applied to open wounds. The medicinal value of extracts has been evident by in vitro/in vivo assay of antioxidant, anti-bacterial, anti-inflammatory, anti-microbial, vasorelaxant, anti-leishmanial and mosquitocidal activities. Still, there is derth in the studies on isolation, characterization and evaluation of active principles from the extracts. This current review article gives comprehensive information about the T. procumbens taxonomy, morphology, geographical distribution, phytoconstituents and pharmacological activities.

KEYWORDS:

Tridax procumbens, Antioxidant, Anti-hepatic, Anti-inflammatory, Anti-arthritic, Anti-microbial, Anti-diabetic, Anti-cancer, Antihypertensive, Immunomodulatory, Wound healing.

INTRODUCTION:

Tridax procumbens is a widely spread hispid, procumbent herb, usually found as a weed. T. procumbens is perennial in nature with flowering-fruiting throughout the year [1-4]. T. procumbens is commonly called as ‘Jayanti-veda’ in Sanskrit, Tikki-kasa/'Ghamra' in Hindi and ‘Wild daisy’, ‘Mexican daisy’ and ‘Coat buttons’

in English based on the appearance of the flower. The scientific name is 'Tridax procumbens' [3-7]. The generic name is derived from the Greek, meaning 'summer eating', implying that it was a summer vegetable [8].

T. procumbens belongs to the kingdom: Plantae, sub-kingdom: Tracheobionta, division: Magnoliophyta–Dicotyledons, class: Magnoliopsida, sub-class: Asteridae, order: Asterales, family: Asteraceae, genus: Tridax L. and species: procumbens [4].

T. procumbens is widely distributed in India up to 2400 m above sea level [6, 9]. The leaves of the plant are used as raw feed toncattle and food additive by humans as well [6]. The leaves have medicinal value and used to treat catarrh, dysentery and diarrhea.The different leaf extracts are used as antiseptic to treat fresh cuts, wounds, burns and in anemia [10]. It also contains hair growth enhancing ability [11, 12].

Aqueous leaves extract posses cardiovascular effect and signif icantly reduces heart rate and blood pressure. Lyophilized aqueous leaf extract showed anti-inflammatory. Leaf juice is useful in dead space wound healing. Seeds are used to check all types of bleeding. Aqueous extract of whole arial part is used as immunomodulator. Dry extract showed antibiotic activity even when formulated in mineral base. action comparable to ibuprofen and aspirin. Whole arial parts have hepatoprotective,antisecretory (antidiarrhoeal) activity. It is active against bacteria, protozoa and fungi.

Plant morphology and cytology :

T. procumbens is a semi prostate, annual, creeper herb with stem ascending to 30-50 cm in height, branched, sparsely hairy and rooted at nodes. Leaves are simple, opposite, serrate or dentate, acute, fleshy, pubescent, exstipulate, lanceolate to ovate in shape with 3-7 cm long, irregularly toothed margin with wedge shaped base, shortly petioled and hairy on both surfaces (fig. 1). The leaves are dorsiventral; epidermis is single layered on both the surfaces and covered with a thick cuticle. Upper epidermis shows single layered, multicellular covering trichome and lower epidermis is single layered, elongated cell and closely arranged [13]. Xylem vessel shows the presence of calcium oxalate crystals. Vascular bundles are concentric in shape. Meristeel consists of single, centrally located collateral vascular bundle surrounded by some parenchymatous cells [13]. Flowers are tubular in nature, yellow in color with hairs having a capitulum inflorescence [4, 13, 14]. This has two types of flowers: ray florets and disc florets with basal placentation [13].

Fruit is a hard achene covered with stiff hairs and having a feathery, plume-like white pappus at one end, which assists in aerial dispersal [4, 13]. The heads are heterogeneous, having long peduncles which may reach up to a height of 2 ft. The ray florets are female with ligulate corolla, trifid and invariably pale-yellow in color [8] (fig. 2). T. procumbens seeds germinate at higher temperatures (35/25 and 30/20 °C) in the presence of 58 to 78 % light. These are very sensitive to salt concentration and water stress [15]. The chromosome numbers are 36 (diploid) and 18 (haploid) in gametes [8]. The propagation is through spreading stems and seed production [4].

Chemical constituents:

T. procumbens contains flavone glycosides, chromone glycosides, sterols and polysaccharides with a Beta-1,6-D-galactan main chain. Unsaponifiable fraction of petroleum ether fraction revealed the presence of campesterol, stigmasterol and beta- sitosterol by GCMS (Gadre and Gabhe, 1992). The ethyl acetate soluble part of hexane extract yielded a new bithiophene named tri-bisbithiophene along with four terpenoids: taraxasteryl acetate, betaamyranone, lupeol and oleanolic acid (Ali and Jahangir, 2002). A new flavonoid (Procumbenetin) isolated from arial part of T. procumbens has been characterized as 3, 6-dimethoxy-5, 7, 2', 3', 4'-pentahydroxy flavones, 7-O-beta-3- glucopyranoside (Ali and Ramachandram, 2001). Eight new compounds, isolated from Tridax procumbens, have been characterized as methyl 14-oxooctadecanoate, methyl 14-oxononacosanoate, 3-methylnonadecylbenzene, heptacosanyl cyclohexane caprylate, 1(2,2-dimethyl-3-hydroxypropyl)-2-isobutyl phthalate, 12-hydroxytetracosan-15-one, 32-methyl-30-oxotetratriacont-31-en-1-ol and 30-methyl-28-oxodotriacont-29-en-1-oic acid by spectral data and chemical studies. Nine known compounds isolated for the first time from the plant, were identif ied as dotriacontanol, amyrone, 12-dehydrolupen-3-one, amyrin, lupeol, fucosterol, 9-oxoheptadecane, 10-oxononadecane and sitosterol (Verma and Gupta, 2004).

Anti-arthritic activity:

Arthritis is an inflammatory disorder involving damage to one or more joints. The ethanolic extract of the T. procumbens displayed a significant role in the anti-arthritic activity in Freund's Complete Adjuvant (FCA) induced rat model compared with that of the standard drug, indomethacin. An evaluation was done by an increase in the body weight, RBC count, Hb level and a decrease in ESR level, WBC count, pannus formation and bone destruction. The rheumatoid arthritis is characterized by loss of articular cartilage leading to diminished joint spaces due to severe swelling of soft tissues through a variety of pathological mechanisms and bone resorption which was normalized by the administration of ethanolic extract of the T. procumbens confirming the anti-arthritic activity of the extract [32].

Antioxidant activity:

The oxygen free radicals generated from phagocytes activates transcription factor NF-κB inducing the formation of inflammatory cytokines and activation of cyclooxygenase-2 (COX-2). This initiates tissue damage cascade mechanism which needs to be neutralized. T. procumbens shows anti-oxidant activity. This was validated by DPPH (2, 2-diphenyl-picrylhydrazyl hydrate) and ABTS [2, 2'-azino-bis (3-ethyl benzothiazoline-6-sulphonic acid)] methods. Chloroform and ethyl acetate fractions of ethanol extract showed maximum activity in DPPH method with IC50 values of 37.39 µg/ml. In addition, methanol extract also showed antioxidant activity in DPPH method [1]. Flavonoids and alkaloids of the extracts are mainly responsible for the activity [17].

Hepatoprotective property:

The liver is the major detoxifying organ in the body. Liver contains enzymes involved in detoxification mechanism. Any injury to the hepatic cells releases the enzymes into the blood stream. The serum marker enzyme estimation gives the extent and type of hepatocellular damage [24]. T. procumbens showed hepatoprotective activity. Lipopolysaccharide and D-galactosamine-induced hepatitis in rat model were significantly decreased by chloroform extract of aerial parts of T. procumbens as evident by the decrease in enzyme markers such as aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase, gamma glutamyl transferase and bilirubin in the serum of the animal model. Thus, the extract ameliorates the hepatocellular injury and initiated parenchymal cell regeneration in the liver [4, 17, 19, 24, 25]. Similar results were also observed with aqueous extract of T. procumbens coupled with chloroquine [20].

Anti-inflammatory activity:

The aqueous, ethyl acetate, methanol and ethanol extracts showed significant anti-inflammatory activity by inhibiting the actions of inflammatory mediators such as histamine, serotonin, bradykinin and prostaglandins [28, 29]. The identified active components Bergenin, Centaureidin and Centaurein from solvent extracts inhibited COX-1 and COX-2 enzymes. The flavonoid compound 'Quercetin' is responsible for analgesic and anti-inflammatory activity. This might also be responsible for the inhibition of inflammatory pain and anti-allodynic effect on chronic constriction injury (CCI) induced neuropathic pain model [30, 31].

Immunomodulatory activity:

The ethanolic extract of T. procumbens has immunostimulatory property as it enhanced the uptake of particulate matter by phagocytes [33]. This also stimulates a cell-mediated immune response by increasing the number of leukocytes, plasma cells and splenic leukocytes in turn increasing the phagocytic index. The active component 'sesquiterpene lactone', majorly present in the ethanolic extract, is known to induce delayed type hypersensitivity reaction. The extract prevents BSA sensitized anaphylactic reaction by producing IgG antibodies blocking the BSA-IgE interaction, thereby inhibiting mast cell degranulation [4, 19, 25, 33]. This was also observed in Pseudomonas aeruginosa infections [34].

Wound healing:

The leaf extract is commonly used in Indian traditional medicine and topically applied on open wound to stop bleeding and enhance the healing process. The plant extract showed wound healing activity in a rat model with increased lysyl oxidase and hexosamine levels that are reported to stabilize the collagen fibres by increasing the crosslinking of collagen during the healing process. The extract also increases mRNA content and protein

synthesis of glycosamine glycan (GAGs) content which are the main components of ECMs in the granulation tissue [4, 19, 22, 25, 35-37].

T. procumbens enhances wound healing by interacting with epidermal cells, dermal cells, ECM, soluble proteins and angiogenesis processes co-ordinated by an array of cytokines and growth factors [38]. The ethanolic extract showed significant wound healing activity in gel based formulation [39]. In excision wound healing process, T. procumbens extract shows indirect corticotropic effects. This increases the tensile strength of collagen fibers and rate of
epithelialization [12, 19, 36, 40]. The leaf extract is also reported to stop bleeding when applied topically [41].

Anticancer activity:

The aqueous extract of T. procumbens leaves containing essential oils showed anti-metastatic activity on lung cancer development in C57BL/6 (B16 F-10 melanoma cell line) mice evidenced by neutralizing the increase in body weight, WBC and hemoglobin count. The active compounds are α-pinene (C10H16), β-pinene (C10H16), phellandrene (C10H16) and sabinene (C10H16), all belonging to monoterpene family. This is characterized by the increased expression of caspase-3 and p53 as analyzed by Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay [42].

The acetone extract of flower showed an apoptotic effect within 24 h of treatment [43-46]. Lupeol, a triterpenoid isolated from dried leaves of T. procumbens plant, gave positive results for in vitro anticancer activity in MTT assay. It showed more than 90% of cytotoxic potential against human lung cancer cell line A-549 by colony formation inhibition assay. The mode of action is through inhibiting COX activity and increasing the DNA fragmentation by activation of endogenous endonucleases causing apoptosis.

Antihypertensive activity:

Increased pulse pressure predicts cardiovascular and coronary artery disease, myocardial infarction (MI) and congestive heart failure, which is independent of diastolic blood pressure and systolic blood pressure. Whereas, the high heart rate (tachycardia) is associated with an increased risk of death from cardiovascular and non-cardiovascular causes [47]. The aqueous extract of the T. procumbens leaves lowered the mean arterial blood pressure and heart rate in the Sprague–Dawley rat models [25, 48].

Vasorelaxant activity:

Smooth muscle contraction is involved in many physiological activities such as blood circulation, organ maintenance and peristalsis of biological tracts. The aqueous extract of T. procumbens leaves induced relaxation of isolated aortic rings from rat by decreasing the calcium supply from the extracellular fluid. The

extract also neutralized the phenylephrine/high potassium induced smooth muscle contraction by NO synthase pathway (either by increasing endothelial production of NO or premature activation of NO production) [50, 51].

Antimicrobial activity:

The extracts of T. procumbens showed anti-microbial activity against gram+ve and –ve bacterial strains. The anti-microbial activity of different extracts is as shown in the table. 1. This explains the reason for using the plant in traditional folk medicine to treat dysentery, diarrhea and gastrointestinal disorders of bacterial infections.

Anti-diabetic activity:

Extracts of T. procumbens (aqueous, methanolic and ethanolic) exhibited anti-diabetic activity. The extracts decreased the alloxaninduced diabetic condition in the Wistar rat animal model by reducing blood glucose level when administered orally for 7 consecutive days [4, 19, 25, 60]. Alloxan causes diabetes by destroying the insulin-producing beta cells of the pancreas. Alloxan is selectively toxic to the beta cells, which induces cell necrosis. The cytotoxic activity of the alloxan is supplemented by the reactive oxygen species and an increase in the cytosolic calcium concentration, leading to the rapid destruction of beta cells [60]. The extracts help in regeneration of pancreatic beta-cells destroyed by alloxan potentiating insulin release and stimulating peripheral glucose utilization or enhancing glycolytic and glycogenic processes by decreasing glycogenolysis and gluconeogenesis [61].

Dihydroxy-olide is an active principle from T. procumbens hexane extract responsible for exhibiting the anti-diabetic effect. This causes a reduction in glucose absorption and lowers the postprandial rise in blood glucose level in Type-II diabetes mellitus [62].

Mosquitocidal:

Alpha-Terpinene, α-Terpineol and β-Pinene, being the major chemical constituents in the essential oil extract from the T. procumbens plant, significantly showed repellent activity against the malarial fever mosquito Anopheles stephensi at 6 % concentration [25, 63].

Waste water treatment:

respectively [65]. The biogenic pure crystalline spherical-shaped silver nanoparticles synthesized from the aqueous extract of T. procumbens leaves showed antimicrobial activity, inhibiting gram positive bacteria, gram negative bacteria and fungal strains [21].

The activated biocarbon derived from the dry powder of T. procumbens leaves are effective in the removal of heavy metal ions [Zn (II) and Cd (II)] from the waste water. The experimental data were in agreement with both Langmuir and Freundlich adsorption isotherm and was much more effective when compared to then standard commercial charcoal extraction method [66]. Similarly, activated carbon from the T. procumbens leaves is an efficient bioadsorbent for removal of hexavalent chromium from synthetic and industrial tannery wastewater [25, 67].

Toxicity induced by T. procumbens:

T. procumbens ethyl acetate extract increased the body weight of experimental animal groups.

CONCLUSION:

T. procumbens is a major medicinal plant used since before recorded history in both organized (Ayurveda, Unani) and unorganized (folks, tribal, indigenous) traditional medicine practices. The Recent technological invention in identifying, isolating and validating active principles from medicinal plants has gained importance as these may provide an excellent source of lead molecules for the treatment of various disease conditions.

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