Medicinal Value of Euphorbia Tirucalli

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ABSTRACT

Natural products play an important role in drug discovery and many approved therapeutics as well as drug candidates have been derived from natural sources. They have been the source of most of the active ingredients of medicines. The beneficial medicinal effects of plant materials typically result from the combinations of secondary products present in the plan. These secondary metabolites constitute the medicinal value of a drug plant, which produces a definite physiological action on human body. The plant of Euphorbia tirucalli belongs to the family Euphorbiaceae, which is commonly known as Barki-thohar. This plant is native of America but has become acclimatized and grows freely in all parts of India. This is a common medicinal plant of India; the plant's milky juice and stem bark are used. Milky juice in small doses is a purgative but in large doses it is acrid, counter-irritant, and emetic. E. tirucalli latex seems to reduce the specific cellular immunity associated with the virus Epstein-Barr injection by activating the virus lytic cycle. The bark/latex of E. tirucalli presents pharmacological activities as anantibacterial, molluscicide, antiherpetic, and antimutagenic. It also shows cocarcinogenic and anticarcinogenic activities. In the northeast of region in Brazil, the latex of E. tirucalli is used as a folk medicine against syphilis. As an antimicrobial; a laxative agent to control intestinal parasites to treat asthma, cough, earache, rheumatism, verrucae, cancer, epithelioma, sarcoma, and skin tumors. E. tirucalli contains a large quantity of terpenes and sterols among its constituent and the following substances, which have been isolated; alcohol eufol, alfaeuforbol, and taraxa sterol e tirucallol (Imai, 1994; This review highlights on the existing information particularly on the phytochemistry and various pharmacological properties of E. tirucalli, which may provide incentive for proper evaluation of the plant as a medicinal agent.

Introduction

In spite of great advances of modern scientific medicine, traditional medicine is still the primary form of treating diseases of majority of people in developing countries including India; even among those to whom Western medicine is available, the number of people using one form or another of complementary of alternative medicine is

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Correspondence: Ms. Nishi Gupta, E-mail: nishi0032@gmail.com rapidly increasing worldwide.^[1] Over the centuries, humans have relied on plants for basic needs such as food, clothing, and shelter, all produced or manufactured from plant matrices (leaves, woods, fibers) and storage parts (fruits, tubers).^[2] Many plant-derived compounds have been used as drugs, either in their original or semisynthetic form.^[3] The World health Organization (WHO) estimates that about 80% of the population living in the developing countries rely almost exclusively on traditional medicine for their primary healthcare needs.^[4] India is the largest producer of medicinal herbs and is appropriately called the botanical garden of the world.^[5] In recent years, the use of herbal medicines worldwide has provided an excellent opportunity to India to look for therapeutic lead compounds from an ancient system of therapy, that is, Ayurveda, which can be utilized for development of new drugs.^[6]

Euphorbia lirucalli (Euphorbiaceae, Euphorbioideae) is considered the second largest genus in the angiosperms, including ca. 2000 species.^[7] The *Euphorbiaceae* family includes trees, succulents, and herbaceous plants.^[8] Different species of *Euphorbia* grow all over the world, either wild, or as cultivated specimens in the house or garden.^[9] Euphorbiaceae is among the large flowering plant families consisting of a wide variety of vegetative forms some of which are plants of great importance.

Its classification and chemistry have of late been subjects of interest possibly because of the wide variety of chemical composition of its members, many of which are poisonous but useful. The worldwide distribution of the family exposes its members, to all sorts of habitats to which they must adapt, therefore inducing a large variety of chemicals (secondary substances) that are employed for survival/ defense.^[10] Euphorbiaceae is generally distinguished by the milky sap.^[11] Euphorbiaceae comprises nearly 322 genera and 8910 species many of which have their own economic value and hence contribute to the floristic wealth of tropical and subtropical countries of the world. The family comprise a number of endemic and endangered taxa.^[12]

About the plant

A large unarmed shrub or a small tree up to 5 m tall with erect branches; bark rough, cracked, greenish brown, exuding a milky sap when cut, branch lets slender, smooth, cylindrical, polished, whorled, and modified into phylloclade.^[13] *E. tirucalli* is probably the best known and most widespread of all tree Euphorbia species.^[14] It is a shrub or a small tree endemic to tropical areas with pencil-like branches from which it derives its vernacular name, the pencil-tree. *E. tirucalli* is generally evergreen since its stems and branches remain green all year round and are rarely fed on by herbivores. It bears white poisonous latex, which may possibly account for the low herbivore pressure and medicinal features.

Taxonomic Description

In the binomial system (USDA plants data at www.plants.usda. gov), *E. tirucalli* L. (ET) belongs to:

Kingdom: Plantae. Division: Magnoliophyta. Class: Magnoliopsida Order: Malpighiales. Family: Euphorbiaceae. Genus: Euphorbia. Species: Euphorbia tirucalli. Binomial name: Euphorbia tirucalli

Vernacular names^[15]

Amharic: Kinchib; Arabic: Knjil; English: Finger euphorbia, Indian spurge tree, milk bush, naked lady, pencil-tree, rubber euphorbia; Filipin: Bali bali; French: Arbre de Saint Sebastien, Euphorbe effile euphorbe, Garde maison, Tirucalli; Malay: Kayu patah, Tentulang, Tulang, Tulang-tulang; Somali: Dana; Spanish: Alfabeto chino, Antena, Esqueleto, Palito, Aveloz; Swahili: Mtupa mwitu, Mwasi, Utupa; Thai: Khia cheen, Khia thian; Ugandan: Kakoni (luganda), Oruyenje (runyankole); Vietnamese: San h(oo) xanh, X(uw) (ow)ng c(as).

Habitat

Commonly planted as an ornamental or hedge plant.^[16] In Hawai'i (Kaua'i), "sparingly naturalized locally as it forms dense thickets along Lawa'i Road where it is propagating vegetatively".^[17] *E. tirucalli* is probably the best known and most widespread of all tree Euphorbia species.^[18] It originated from tropical East Africa and it is endemic in countries such as Angola, Eritrea, Ethiopia, Kenya, Malawi, Mauritius, Rwanda, Senegal, Sudan, Tanzania, Uganda, and Zanzibar. The same authors intimate that the tree is currently widely distributed in southern Europe, Asia, and the Americas having been steadily introduced due to its ornamental and medicinal features. *E. tirucalli* can survive in a wide range of habitats.^[19,20] Plant can grow under conditions in which most crops and other trees cannot grow. They include: Tropical arid areas with low rainfall, on poor eroded soils, saline soils, and high altitudes up to 2000 m but cannot survive frost. Its distribution is therefore limited by low temperatures.^[21]

Botanical description

ET is a succulent, cactus-like (FAO) spineless, unarmed, muchbranched, monoecious or more often dioecious, easy to recognize, perennial shrub, or tree up to 10-15 m tall.

Trunk or stem

The rubber-hedge euphorbia reach usually 2-5 m but may grow up to 15 m on occasion with a 2-4 m spread. The main trunk and branches are woody and brownish and may thicken up to a diameter of 25 cm. It grows with single or multiple trunks. The bark of very old specimens is gray and rough with longitudinal dents and ridges that break up into very small fragments. There are sometimes conspicuous, small protuberances, such as a bulge, knob, or swelling, on the bark, and occasionally black, rough, crosswise bands.

Branches

E. tirucalli is a plant very branched with branches often arranged in pseudo whorls10 forming brush-like masses that are the best known feature of this species.

Leaves

Leaves are rarely seen as they fall very early o quickly (early deciduous), tiny, few, simple, fleshy, small or minute, slender, and alternate. The leaf blade is linear-lanceolate to oblanceolate, 1-2.5 cm long, 3-4 mm broad, and 2 mm thick, acute at tip, tapered to the sessile base, arranged spirally, present only at the tips of young branchlets. The extreme tips of young leafy branchlets are sparsely tomentose, with curled brown hairs, and soon glabrescent. Stipules are minute, glandular, and dark brown. The function of the leaves is taken over by the green branches.

Flowers

Plants are monoicous or dioicous, the chromosome number is 20 and the diploid number is 2n. The flowers are small or very small, yellow, green, or pink arranged in groups on the terminal branches, discreet, and grouped at the top of the short branches, in heads, stalkless at the end of twigs, and carried in clusters at the apex of the short branches or in the angles of branches.

Fruits

Fruits are tripartite capsule and a capsule measures about 8-12 mm in diameter, is subglobose (nearly globose), almost glabrous or glabrescent, longitudinally very slightly lobed, short-stalked (8 mm), bent at an angle, pale green, with a pink tinge and conspicuously pubescent (soft hairs). Capsules dehisce while still on the tree, and exerted on a tomentosepedicelto 1 cm long.

Seeds

The seeds are ovoid (oval), about $3-4 \times 2.8-3$ mm, glabrous, smooth, buff speckled with brown and with a dark brown ventral line (with a white line), around the small white caruncle 1 mm across.

Latex

The latex is a caustic milky white sap when damaged, like many other Euphorbia species.

Root system^[22]

The plant produces lateral roots that do not grow very deep [Figure 1].

Phytoconstituents of Euphorbia tirucalli

Euphorbiaceae plants store abundant amounts of latex in an organ called the laticifer.^[23] The major constituents of latex are isomers of triterpenes with the molecular formula $C_{30}H_{50}O$ (MW: 426), such as euphol, tirucallol, glut-5-en-3-b -ol, cycloeuphordenol, euphorginol, aamyrin, lanosterol, cycloartenol, and others^[24-27] [Table 1].12,20-Dideoxyphorbol-13 isobutyrate, 12-deoxy-4 β -hydroxyphorbol-13-phynylacetate-20-acetate and euphol isolated from latex, glut-5-en-3 β -oland cycloart-23-en-3 β , 25-Diolisolated from stem bark, a new macrocyclic diterpene tirucalicine isolated from latex and its structure determined, isolationand characterization of 31-nortriterpene-cycloeuphordenolfrom latex, a new triterpenes cyclotirucanenol isolated and its absolute configuration is determined, euphorginol isolated from the stem bark and its stereo structure determined.^[28]

Plant extract

Extraction, as the term is used pharmaceutically, involves the separation of medicinally active portions of plant or animal tissues from the inactive or inert components by using selective solvents in standard extraction procedures. The purposes of standardized extraction procedures for crude drugs are to attain the therapeutically desired portion and to eliminate the inert material by treatment with a selective solvent known as menstrum. The extract thus obtained may be ready for use as a medicinal agent in the form of tinctures and fluid extracts, it may be further processed to be incorporated in any dosage form such as tablets or capsules, or it may be fractionated to isolate individual chemical entities such as ajmalicine, hyoscine, and vincristine, which are modem drugs. Thus, standardization of extraction procedures contributes significantly to the final quality of the herbal drug. General Methods of Extraction of Medicinal Plants-Maceration, Infusion, Digestion, Decoction,

Percolation, Hot Continuous Extraction (Soxhlet), Aqueous Alcoholic Extraction by Fermentation, Counter-current Extraction, Ultrasound Extraction (Sonication), Supercritical Fluid Extraction, and Phytonics Process.^[29] *E. tirucalli* can be extracted in methanol, chloroform, pet ether, acetone for various activities.

Ethnomedicinal uses

Just like the complexity in classification, ethnomedicine of Euphorbiaceae is very diverse. This diversity is due to the presence of a wide range of unusual secondary metabolites that makes most of the members poisonous.^[30] In addition, some members are said to cause or influence susceptibility to certain body ailments. For example, *E. tirucalli, E. leuconeura*, Jatropha curcas and others are known to be cocarcinogenic and can influence/promote excessive cell division resulting in tumor growth.^[19,20,31,32] Also latex of *E. tirucalli* and *E. royleanais* known to cause conjunctivitis on contact with eyes.^[33,34] In the northeast region of Brazil, the latex of *E. tirucalli* is used; as an antimicrobial agent; a laxative agent; to control intestinal parasites; to treat asthma, cough, earache, rheumatism, verrucae, cancer, chancre, epithelioma, sarcoma, skin tumors, and as a folk remedy against syphilis.^[20]

Uses

Traditional medicine

Possibly due to a great variety of chemical substances found in *E. tirucalli* tissues, medical folklore literature of different parts of the world (especially tropical and subtropical areas where it is endemic) is tainted with its curative ability. In East Africa, latex is used against sexual impotence, warts, epilepsy, toothache, hemorrhoids, snake bites, extraction of ecto-parasites, and cough among others. In Peninsular Malaysia, a poultice of the roots or stems is applied to nose ulceration, hemorrhoids, and swellings. Root scrapings mixed with coconut oil are taken for stomach ache.^[19,20] In India, it is an unavoidable plant in most traditional homesteads and used as a remedy for ailments such as: Spleen enlargement, asthma, dropsy, leprosy, biliousness, leucorrhoea, dyspepsia, jaundice, colic, tumors, and bladder stones. The latex of vesicant and rubifacient is emetic in large doses, it is purgative in small doses and applied against toothaches, earaches, rheumatism, warts, cough, neuralgia, and



Figure 1: Euphorbia tirucalli^[22]

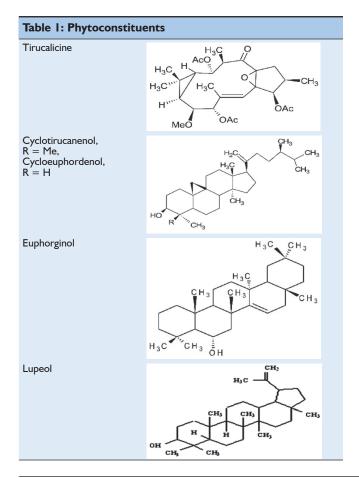
scorpion bites. The same author points out that its branch and root decoctions are administered for colic and gastralgia while ashes are applied as caustic to open abscesses.^[35] In Brazil, *E. tirucalli* is used against cancer, cancroids, epitheliomas, sarcomas, tumors, and warts, although they argue that this has no scientific basis since the same tree is known to be cocarcinogenic. In Malabar (India) and the Moluccas, latex is used as an emetic and antisyphilitic, whereas in Indonesia, the root infusion is used for aching bones while a poultice of roots or leaves is used to treat nose ulcers, hemorrhoids, and extraction of thorns. Wood decoctions are applied against leprosy and hands and feet paralysis following childbirth. The same author states that in Java, the plant latex is used to cure skin ailments and bone fractures.^[19,36]

Ornamental

E. tirucalli has increasingly become popular as an ornamental plant. Potted plants are placed in offices and homes but can also be grown in lawns. It is preferred for its ease of maintenance and beautiful evergreen pencil-like branches, which factors have increased its international trade resulting into a wide distribution in areas where it was not endemic.

Source of energy

It was reported that latex of *E. tirucalli* is composed of petroleum like hydrocarbons largely C_{30} triterpenoids, which on cracking, yield high-octane gasoline. It was estimated that a crude gasoline yield between 4 and 8 barrels per hectare from an *E. tirucalli* planted field



per year; and calculated at about 3 dollars per barrel, it is three times cheaper than normal crude oil.^[37-39] E. tirucalli is still looked at as a potential source of biodiesel as it can produce a high biomass and grow in marginal areas unfit for production of other crops. Of late, there has been increasing attention on biodiesel production in order to reduce overdependence on fossil fuel.^[40] Associated with biodiesel production is methane and biogas generation; many scientists, considering its reported high biomass production and ease with which it ferments, note that it is a potential source of methane and biogas.^[41,42] It was experimentally demonstrated that *E*. tirucalli produces suitable biomass for biogas generation especially through chopped material under thermophilic conditions, which can yield 1.06 l/day of biogas in just 19 days.^[43] For the same reason, it has been recommended for commercial fuel wood production projects for purposes of woodlot restocking in semi-arid parts of Kenya.^[44] E. tirucalli is preferred for this purpose due to its fast growth rate, high productivity, quick acclimatizion to an area, and ease with which it dries.

Source of rubber

E. tirucalli is reported for possessing hydrocarbon polymers that are used for manufacturing rubber substitutes. Several researchers point out that its latex is an emulsion of terpenes and resins in water, which can easily be transformed into rubber at low cost.^[37,41,45] Also, due to the strong fixative power of the resin, it has for long been used on the East African coast in local gum manufacture for fastening knife-blades to wood handles and spear-heads to shafts.^[19] The resin produces comparably good wood-based glue and adhesives whereas with a few modifications, it would compete favorably with other commercial resins.^[46]

Conservation and agroforestry

Due to its favorable agronomic features such as drought resistance, *E. tirucalli* is used in semi-arid areas to carry out afforestation and reforestation for purposes of achieving soil conservation. These plants can be used as a soil cover in places where other plants (even grasses) cannot grow.^[21] Involvement of *E. tirucalli* has been mentioned in successful reforestation and conservation programs in: Tanzania,^[47] Kenya,^[41,48] and Sri Lanka^[49] among others. It has also featured in agroforestry programs^[50-52] as a hedge plant or as an intercrop. Other related uses of *E. tirucalli* include: Boundary demarcation,^[19,53] live fencing around compounds and kraals,^[19,54,55] cultural connotations, for example, as a sign of starting a new home in Luo culture of East Africa^[44] and as a windbreak in semi-arid areas,^[56] Plant plays these roles due to its latex toxicity and hence low herbivore pressure.^[55]

Pesticides

E. tirucalli latex has been reported to have pesticidal features against such pests as aphids (Brevicoryne brassicae),^[57] mosquitoes (Aedes aegypti and Culex quinquefasciatus),^[58] microorganisms such as bacteria (*Staphyloccoccus aureus*)^[59] and molluscs (Lymneae natalensis) and Biomphalaria gabrata^[60] among others. A dose dependent latex toxicity to parasitic nematodes was also reported such as Haplolaimus indicus, Helicotylenchus indicus, and Tylenchus filiformis *in vitro*, with increasing exposure period, although some nematodes like Meloidogyne spp. are known to attack the plant.^[61] The latex is also reported to be a hunters' tool applied in local fishing and arrow poisoning in tropical Africa.^[62] Piscicidal feature

has been validated.^[60] Although the plant is generally mentioned as a pesticidal plant; scanty experimental work has been performed to confirm this.

Pharmacological activities

- 1. Oxytoxic activity: Latex of this plant showed strong oxytoxic activity against isolated strips of the gravid ratuterus.
- 2. Antiarthritic activity: The biopolymeric fraction (BET) from plant *E. tirucalli* Boiss (Euphorbiaceae). The fraction showed dose dependent antiarthritic activity and also showed *in vivo* immunomodulatory capacity being a major component in inhibiting arthritis. It caused suppression of CD4+ and CD8+ T cells, inhibition of intracellular interleukin-2 (IL-2) and interferon-gamma (IFN-_) by flow cytometry.^[28]
- 3. Molluscicide activity: An aqueous solution of the latex of *E. tirucalli* collected at sites receiving large amounts of sunlight showed molluscicide action on Biomphalaria glabrata, with LD50 obtained at the concentration of 28.0 ppm and LD90 at the concentration of 85.0 ppm. The toxicity of the product for fish was similar to that of Bayluscide and of copper sulfate used for comparison. However, the wide distribution of the plant, its easy propagation, and the simple procedure for extraction of the active substance, which is biodegradable, favor "avelos" as a promising agent in the control of schistosomiasis.^[63]
- Antimicrobial activity: Acetone extracts of the stem of E. tirucalli 4. were inhibitory to all the test microorganisms. Escherichia coli was found to be highly sensitive to the acetone extracts of E. tirucalli. The MIC was 500 µg for Candida albicans and 750 µg for Aspergillus niger and A. fumigatus. The chloroform extracts of the stem of E. tirucalli are active against B. subtilis, E. coli, Proteus vulgaris, S. aureus, A. niger, and C. albicans and the minimum inhibitory concentration was 250 µg for P. vulgaris, 500 µg for E. coli and S. aureus, whereas it was 750 µg against Bacillus subtilis and C. albicans, 1000 µg for A. niger. The methanol extracts of the stem of E. tirucalli showed activity against B. subtilis, E. coli, E. faecalis, S. aureus, and C. albicans and its minimum inhibitory concentration was found to be 500 µg for E. coli and S. aureus, whereas it was 750 µg for B. subtilis, E. faecalis and 1000 µg for C. albicans. The petroleum ether and hexane extracts did not show activity against the test organisms.^[64]
- 5. Antiherpetic activity: To evaluate the capacity of the extracts to inhibit the lytic activity of herpes simplex virus type 2 (HSV-2) and the reduction of viability of infected or uninfected cell cultures, the end-point titration technique (EPTT) and the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] colorimetric assay were used, respectively. The therapeutic index of the positive extracts for the antiviral activity was determined by calculating the ratio CC (50% cytotoxic concentration) over IC50 (50% inhibitory concentration of the viral effect). Five of the 47 extracts (11%) representing 3 out of 10 Euphorbia species (30%) exhibited antiherpetic action; the highest activity was found in the leaf/stem water-methanol extracts from *E. cotinifolia* and *E. Tirucalli*.^[65]
- 6. Antioxidant Activity: A systemic and scientific investigation of aqueous extract of *E. tirucalli* for its antioxidant, Antioxidant property was assessed by using reducing property, superoxide anion scavenging and hydroxyl radical scavenging property. The aqueous extract has demonstrated dose-dependent *in vitro* antioxidant property (at 20, 40, 60, 80, 100 µg) in all the models of the study.

- 7. Hepatoprotective Activity: A systemic and scientific investigation of aqueous extract of E. tirucalli for its hepatoprotective potential against carbon-tetrachlorideinduced hepatic damage in rats was carried out. Hepatoprotective property was assessed by measuring the extent of reversal of enhanced biochemical markers of hepatitis, like serum glutamate pyruvate transaminase, serum glutamate oxaloacetate transaminase, alkaline phosphatase (ALP), biluribin, cholesterol, triglycerides, and also by estimating the tissue glutathione (GSH) levels and the extent of reduction in the tissue lipid peroxidation. Similarly, aqueous extract of E. tirucalli at the doses of 125 and 250 mg/kg produced significant hepatoprotective effect by decreasing the serum enzymes, bilirubin, cholesterol, triglycerides, and tissue lipid peroxidation, while it significantly increased the levels of tissue GSH in a dose-dependent manner.[66]
- 8. Immunomodulatory activity: Myelo suppression concomitant with increased numbers of spleen CFU-GM was observed in tumor-bearing mice. Treatment of these animals with ET (125, 250, and 500 mg/kg) stimulated marrow myelopoiesis and reduced spleen colony formation, with no differences observed between the effects of the three doses. The changes produced by the tumor in total and differential marrow cell counts were restored by the treatment with ET. Prostaglandin E2 (PGE2) levels, which were dramatically increased in tumor bearers, was also abrogated by the treatment with the plant extract. ET significantly enhanced survival and concurrently reduced tumor growth in the peritoneal cavity.^[67]
- 9. Cytotoxic and Antiviral Activities: Forty-seven plant extracts of 10 species of the genus Euphorbia (Euphorbiaceae). The capacity of the extracts to inhibit the lytic activity of herpes simplex virus type 2 (HSV-2) and the reduction of viability of infected or uninfected cell cultures, the EPTT and the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] colorimetric assay were used, respectively. The therapeutic index of the positive extracts for the antiviral activity was determined by calculating the ratio CC50 (50% cytotoxic concentration) over IC50 (50% inhibitory concentration of the viral effect). The highest activity was found in the leaf/stem water methanol extract of *E. Tirucalli.*^[65]

Disuses

A number of disuses have also been mentioned. Associated with its vesicant and rubifacient features, E. tirucalli latex is reported to cause conjunctivitis^[68-71] when it accidentally gets in contact with the eyes. Symptoms range from mild epithelial keratoconjunctivitis to severe keratitis with stromal edema, epithelial sloughing, and anterior uveitis, which usually heal in 2-7days but can also result into permanent blindness. It should be handled with caution. Research also shows that E. tirucalli is cocarcinogenic.[72] It was observed that papillomas and malignant tumors were elicited in mice treated with acetone extracts of Euphorbia lattices.[73] Mizuno reports a high incidence of Burkitt's lymphoma-a latent Epstein-Barr virus (EBV) malignancy in East Africa where E. tirucalli is endemic. EBV causative factors were detected in soil and drinking water (where E. tirucalli grows) implying that people living in such areas run a high cancer risk.^[74] The findings have been further clinically validated in rats;^[75-78] some of which developed full blast lymphomas. However, folklore reports anticancer treatment by the latex,^[79] and there are scientific indications that it may modulate myelopoiesis and enhance resistance against tumor bearing,^[80] both of which are suggestive of a cancer cure.

E. tirucalli is known to be an irritant to herbivores and due to its nasty and acrid features, most herbivores learn to avoid it. This is one of the reasons why it is a good live fencing material. Evidently, quite a lot has been done on exploration of its chemistry and evaluation of its potential as an energy plant. However, most of the medicinal uses mentioned have been left to folklore and need validation. For example, in spite of the vast number of ailments it is reported to cure, to our knowledge, no substance of pharmaceutical importance has so far been obtained from it. Also scanty literature has been cited on validation of other functions like the reported insecticidal, nematicidal, piscicidal, and molluscicidal features. This calls for more research/laboratory investigation, in order to establish scientific authenticity of these important functions and to ascertain with confidence that E. tirucalli is a wonder plant for modern science. It remains a research issue whether people should continue to use E. Tirucalli for the mentioned uses but as it were, many societies have always applied it and will continue to do so until its effects are scientifically proved dangerous.[55,81]

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