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Euphorbia tirucalli L.: Review on morphology, medicinal uses, phytochemistry and pharmacological activities

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ABSTRACT

The intention of current review is to make available up-to-date information on morphology, ecological biodiversity, medicinal uses, phytochemistry and pharmacological activities on different parts of *Euphorbia tirucalli* (*E. tirucalli*). This plant has a number of medicinal uses. Latex of *E. tirucalli* is vesicant and rubefacient which is used for rheumatism, warts, cough, asthma, ear-ache, tooth-ache and neuralgia. It acts as a purgative in small doses while in big doses it is bitter irritant and emetic. Milky juice is alexiteric, carminative and purgative. It is useful in whooping cough, gonorrhea, asthma, leprosy, dropsy, dyspepsia, enlargement of spleen, colic, jaundice and stone in bladder. The fresh milky juice is good alternative in syphilis and a good application in neuralgia. A decoction of branches is used in gastralgia and colic. Bark is used in treatment of fractures. Poultices prepared from the stem are useful to repair the broken bones. Boiled root liquid acts as an emetic in cases of snake-bite and for infertility in women. The wood is used for rafters, toys and veneering purposes. It is also useful against leprosy and foot paralysis subsequent to childbirth. *E. tirucalli* is reported to have euphol, β-sitosterol, euphorbol hexacosonate, cycloeuphordenol, cyclotirucanenol, tirucalicine, tri-methyl ellagic acid, gallic acids, terpenic alcohol, isoeuphorol, taraxasterol, tirucallol, euphorone, euphorcinol, euphorbins, 12-deoxy-4β-hydroxyphorbol-13-phenyl acetate-20-acetate, 12, 20-dideoxyphorbol-13-isobutyrate, glut-5-en-3-β-ol, 3,3′-di-O-methylellagic acid, euphorbin-A (polyphenol), tirucallin-A (7) (tannin), tirucallin-B (11), euphorbin-F (14) (dimers), cycloartenol, 24-methylenecycloartenol, ingenol triacetate, 12-deoxy-4β-hydroxyphorbol-13-phenyl acetate-20-acetate, taraxerone, euphorginol, taraxerol, campesterol, stigmasterol, palmitic acid, linoleic acid, β-amyrin, *etc*. active phytoconstituents. *E. tirucalli* have possessed activity in human-lymphocytes, analgesic, anthelmintics, antiarthritic, antibacterial/antifungal/antimicrobial, anti-HIV, anti-inflammatory, antioxidant, antiviral, biodiesel production, CNS depressant/neuropathic pain, cytotoxicity/anticancer, genotoxic/mutagenic, hepatoprotective, insect repellants, immunomodulatory, larvicidal, molluscicidal/ovicidal/piscicidal, myelopoiesis, proteolytic/chitinolytics pharmacological activities. There is a need to isolate dynamic constituents, their biological trial, molecular mechanisms, experimental protection and legalization of therapeutic uses of *E. tirucalli*. The collected information will be helpful to locate up study protocol for recent drugs and Ayurvedic formulation expansion in curative and treat a variety of ailments.

1. Introduction

Euphorbia tirucalli (*E. tirucalli*) Linn. sp. Pl. 452.1753 belonging to Euphorbiaceae family. It is a flowering shrub or tiny tree indigenous to temperate regions. It has pencil like twigs from which it derives its vernacular name pencil tree [1]. Studies revealed that several Euphorbiaceae plant are really effective as therapeutic agent and their active chemical constituents could be isolated and patented as new drugs [2,3]. *E. tirucalli* is broadly distributed in hotter parts of India and planted as a hedge

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plant in garden and along cultivated fields [4]. *E. tirucalli* is universally known as Aveloz. It is a native of Africa and America but has turn out to be acclimated and growing liberally in all parts of India particularly in the drier parts of Bengal and South India and basically grown-up in hedge. It is developed in Berar for shelter young mango plants from straight sunlight [5–7]. The taxonomy of *E. tirucalli* consist of domain: Eukaryota, kingdom: Plantae, sub-kingdom: Tracheobionta, division: Magnoliophyta, super-division: Spermatophyta, class: Magnoliopsida, sub-class: Rosidae, order: Malpighiales, genus: Euphorbia, family: Euphorbiaceae, species: *tirucalli* Linn. [8,9]. The methodology was used for information assortment of this review by searching the keywords '*Euphorbia tirucalli*', 'Thuvar', 'Barki-sehund' 'Pencil tree', 'Finger euphorbia', 'Naked lady', 'Pencil tree' along with different Ayurvedic reference texts, Indian classical books, journals and pharmacopoeias by online and offline database intended for with no definite timeline. The comprehensive information on *E. tirucalli* has been compiled physically from the year 1967–2016 and was set consequently. The present review provides a critical appraisal on morphology, ecological biodiversity, medicinal uses, phytochemistry and pharmacological activities.

2. Occurrence and distribution

E. tirucalli is a resident of Africa and America but has turned out to be acclimatizing and grows liberally in all parts of India particularly in the drier parts of Bengal and South India and basically grown-up in hedge. It is developed in Berar for shelter young mango plants from straight sunlight [5–7]. *E. tirucalli* is almost certainly the most excellent identified and mainly wide-ranging of all trees of *Euphorbia* species [10]. It was invent from hot East Africa and widespread in country like Angola, Ethiopia, Eritrea, Malawi, Kenya, Rwanda, Mauritius, Sudan, Senegal, Uganda, Tanzania and Zanzibar and unusual at Brazil, Indonesia, India, Malaysia, Vietnam, Philippines. In numerous hot areas *E. tirucalli* is growing naturally and usually in deserted site of homesteads and kraals somewhere they form broad timbered plants nurture towards a forest [11,12].

3. Morphology

3.1. Whole plant

E. tirucalli is a flowering shrub or tiny tree which can grow up to (4–12) m tall and about (15–20) cm in stem width with straight twigs. It is smooth, cylindrical, terete, polished, whorled branchlets not much thicker than a quill which bear in the rainy season.

3.2. Leaves

Leaves are small linear-oblong, spotted and oblanceolate about (1.3–2.5) cm lengthy and 2 cm broad. They are nearby only at tips of youthful branchlets and extremely rapidly deciduous, great tips of young leafy branchlets lightly tomentose among rounded coffee hairs.

3.3. Branches

Branches are longitudinal, evergreen and juicy concerning 7 mm wide and typically bent in whorl.

3.4. Stem or trunk

Fresh stems are green, cylindrical with 0.5–2.0 cm in diameter oozes out milky exudates on breaking. Dried stems are greenish brown and surface longitudinally finely striated. Fractures are short and fibrous. Taste is acrid and odor is not characteristic. Transverse section of stem has circular outline exhibiting small notches at some places due to sunken stomata. The epidermal cells are barrel shaped, thin walled filled with rhomboidal crystal of calcium oxalate and covered with thick cuticle. Cortex is broad, parenchymatous outer 3–6 layered chlorenchymatous. The pericycle is characterized by the groups of isolated fibers and laticiferous canal. The phloem is a 5 to 7 cells large consisting of strainer tube and companion cells and uni- to bi-seriate medullary rays in continuation with those of xylem. Xylem is a continuous ring consists of radially arranged vessels, tracheids fibers and parenchyma. Laticiferous canals transverse throughout the cortex, phloem and pith region. Stem stomatal rate of recurrence is predictable at 12 per mm^2 in groove on older stem parts whereas it might accomplish 40 per mm^2 on a soft younger part of stem. Older stems are turn into bumpy, brown and drop their photosynthetic capacity by means of age. Glands are 5–3, transversely oval peltate covered with hair. The bracteoles are abundant and lacerate. Female are woolly. Styles are short, re-curved and bi-lobed. Capsules having 5 mm and cicci compressed like velvet. Seeds are ovoid, 3.5 mm × 2.8 mm in size, soft, buff-speckled and in the midst of a shady coffee ventral line.

3.5. Powder

Powder of stem-bark is yellowish-brown. It is showing fragments of laticiferous canals, lignified fibers, epidermal cells filled with rhomboidal crystals of calcium oxalate and tracheids with bordered pits. It shows rust color with concentrated acetic acid and green color with 1 N hydrochloric acid under UV 366 nm.

3.6. Flowers

Flowers are very tiny, fair, bottle green prearranged in group lying on terminal twigs, judicious and group at the tip of small branches. Cymes are 2–6 overcrowded at the apex of the branchlets. The forking is 2–4 times with heat less than 1 mm extended producing a thick cluster of cyathia which increasing only chaps flowers. Plants usually produce male flowers. Female involucres are consisting of bracteoles present and rarely a small number of chaps' flowers. The perianth is distinctly 3-lobed below the tomentose ovary with 0.5 mm long lobes. Styles are 2 mm long and united at the support with thicken extremely bifid re-curved apex. *E. tirucalli* produces flowers in October and fruits are commencing in November to December. It is pollinated through the insects.

3.7. Fruits

Fruit is glabrescent capsule on top of a tomentose pedicel to 1 cm lengthy and yellowish red while ripe and drop off simply. They have tripartite capsule and it dealings about (8–12) mm in width. Capsules are dehiscing even as still on the tree.

3.8. Seeds

Seeds are oval an about (3.0–4.0) × (2.8–3.0) mm dimension, soft, glabrous, buff spotted with brown and with a dark coffee ventral line around the little fair caruncle.

3.9. Gum/latex

Sap has well-built adhesive power and used at east African coastline for binding knife-blades to timber handle and spear-head to shaft. Latex is a caustic milky white sap.

3.10. Roots

Plant produces lateral roots to not grow up extremely profound.

3.11. Wood

The wood is white, close grained and quite rigid [4,7,12–15].

4. Ecological biodiversity

Ecological biodiversity is required for better cultivation and farming of *E. tirucalli*. It is usually created in dried up bush soil.

4.1. Biophysical limit

Height is up to 2000 m requires for growing up roughly at all types of soil.

4.2. Tree organization

Its coppice is healthy at (20–30) cm altitude. Re-growth of the finger euphorbia is tremendous and underneath partially in arid surroundings. The density of 10 000–20 000 undergrowth is usual after mature as a petroleum crop. It has planted at a spacing of 1 m × 1 m that produced 120 ton/hectare fresh material and 14 ton/hectare dry matter after 1 year which is producing (40–88) kg of crude oil, (135–213) kg of sugar and 1.8 ton of biogases.

4.3. Germination

It is usually epigeous [12].

5. Medicinal uses

5.1. Traditional use

5.1.1. Whole plant

In India, it is useful in treatment of biliousness, leprosy and leucorrhea. In Brazil, it is used against cancroids, cancer, sarcomas, tumors, *etc*. [12,13,16].

5.1.2. Latex

Latex of *E. tirucalli* is vesicant and rubefacient which is used for rheumatism, warts, cough, asthma, ear-ache, tooth-ache and neuralgia. It acts as a purgative in small doses while in big doses it is bitter irritant and emetic. Latex is poisonous to rats and fish. Milky juice is acrid counter-irritant and emetic in large doses. Externally it is rubefacient [5,7]. In Java country, latex is used to heal skin ailment and bone fracture. In Malabar of India and Moluccas, the latex is used as an emetic and an anti-syphilitic. Oil obtained from the latex was in the past used in linoleum, oil skin and leather cloth industry. Methane gas can be formed by anaerobic fermentation of latex [12]. Milky juice is alexiteric, carminative and purgative. It is useful in whooping cough, gonorrhea, asthma, leprosy, dropsy, dyspepsia, enlargement of spleen, colic, jaundice and stone in bladder. The fresh milky juice is good alternative in syphilis and a good application in neuralgia. In Kokan, it is given as a purge [13]. In East Africa, latex is used against tooth-ache, sexual impotence, hemorrhoids, epilepsy, snake bites and cough [16,17]. The sap is irritating to the human eye and causes kerato-conjunctivis and uveitis from the sap of *E. tirucalli*. The eyes of dogs are exposed to the sap of *E. tirucalli* causes corneal opacities which is appeared after (24–36) h and cleared in one to three weeks [18].

5.1.3. Branches

Little twigs of plant can be roast and chew for tender throat [12]. A decoction of branches is used in gastralgia and colic. Ash is useful as caustic to release abscess [19].

5.1.4. Bark

Bark is used in treatment of fractures [5].

5.1.5. Stem

Poultices prepared from the stem are useful to repair the broken bones [12].

5.1.6. Root

Roots are administered in colic and gastralgia [5]. Boiled root liquid acts as an emetic in cases of snake-bite and for infertility in women [12]. Root is used in La Reunion as a vesicant and more rarely as an emeto-cathartic [13].

5.1.7. Wood

The wood is used for rafters, toys and veneering purposes. It is giving a charcoal for use in gun powder [7]. Wood decoctions are useful against leprosy and foot paralysis subsequent to childbirth [12].

5.2. Decorative use

Potted *E. tirucalli* are positioned in office and home however can also be developed in lawns [15].

5.3. Resource of rubber, glue and adhesives

Latex is act as emulsion of concerning 30 percent terpenes in water. During Second World War, the latex was used in South Africa in the improvement of a rubber alternate but this prove to be unbalanced and unbeneficial owing to high latex resin substance [12]. *E. tirucalli* is a resource of rubber and has obsessed hydrocarbon polymers with the intention of industrialized rubber substitute [20–22]. Resin is produces good quality of glue and adhesive [23].

5.4. Resource of energy

Latex of *E. tirucalli* have been reported to compose a fuel like hydrocarbons fundamentally C-30 triterpenoids which on crack yields high octane petrol. It was predictable to facilitate crude petrol that give up 4 to 8 barrels per hectare per year and considered about 30 USD per barrel. It was 30 times cheaper than ordinary basic oil [20,24,25]. There has been rising interest on biodiesel manufacturing in order to decrease overdependence on fossil petroleum [26]. *E. tirucalli* is a prospective resource of methane and biogas too [21,27]. It also produces biomass for biogas generation throughout chopped matter underneath thermophilic environment that can give up 1.06 L/day of biogas [28]. Therefore, it has been suggested for marketable fuel for wood invention project for the purpose of woodlot restock in semi-arid part of Kenya [29].

5.5. Use as protection and agro forestry

E. tirucalli is a complimentary agronomic feature like drought fighting [11]. Contribution of *E. tirucalli* was mentioned in victorious reforestation and protection program in Tanzania [30], Kenya [11,31] and Sri Lanka [32]. It has furthermore feature in agro forestry program [33–35], border line differentiation [16,36], live framework in the order of compound and kraals [16,37,38] artistic connotation at East Africa [29] and wind break in semi-arid area [33]. Plant is playing these roles due to its latex toxicity [38].

5.6. Use as pesticide

Latex of *E. tirucalli* comprises pesticide features against pests like *Brevicoryne brassicae* (Aphids) [39], *Aedes aegypti* and *Culex quinquefasciatus* (Mosquitoes) [40], micro-organisms *Staphylococcus aureus* (Bacteria) [41] and *Lymnaea natalensis* (Mollusks) and *Biomphalaria glabrata* [42]. Dosage reliant latex toxicity to parasitic nematodes like *Hoplolaimus indicus*, *Helicotylenchus indicus* and *Tylenchus filiformis* has been reported [43]. Latex is also reported to be a hunter utensil useful in confined fish and projectile poison in hot Africa [44]. Pesticides characteristic have been validated [45].

5.7. Other uses

E. tirucalli has been used broadly as hedge plant in rural area of East Africa as an obstacle or hold up or border line. It has number of cultural implication in many African communities [12].

6. Phytochemistry

E. tirucalli have contained white milky latex in every piece of the shoot. The principle element of the dried up latex of *E. tirucalli* is a brittle, lustrous resin, resembling rosin in appearance and melting between 65 °C and 75 °C. The possibility of using the resin in the varnish industry has investigated in the Imperial Institute, London. It was found that resin-linseed oil compositions were too slow drying at ordinary temperatures even with abnormally high drier content. The defect could be ameliorated by stoving. More recent work has shown that the resin is subjected to distillation with super-heated steam at 250 °C. The part of these distils is over as a viscous liquid and leaving the major part (90%) of the resin as a dark, brittle, lustrous residue. It is melting in between 125 °C and 145 °C and soluble in benzene, linseed oil and turpentine. Linseed oil varnishes is containing hard resin that gave tack-free glossy films indicating the possibility of its use in the formulation of paints and varnishes. This plant is reported to contain flavonoids, diterpene, steroids, alkaloids and tannins as key phytoconstituents [45]. Chemical compositions of the different parts of *E. tirucalli* have been broadly studied. The whole plant was afforded to include 7.4 percent citric acid with succinic acid and malonic acid. Sterols and terpenoids are the chief source of steroidal compounds, vitamins, anticancer drugs and insecticides [46,47]. It also contains terpenes, alfa-euforbol and alcohol eufol [48], tirucallol, taraxasterol, *n*-hexacosanol and cycloeuphornol [49]. The *E. tirucalli* has been reported to have physical and chemical constituents in its various parts as summarized in Tables 1 and 2, respectively.

7. Pharmacological activities

7.1. Activity in human-lymphocytes

The effects of 14 extracts from 70 plants of Euphorbiaceae were studied using prime immune cell culture by Doris *et al.* [75]. A peripheral blood mononuclear cell (PBMC) exposed to extract phyto-hemagglutinin-A or cycloheximide as agent with the intention to provoke proliferation in PBMC. 14 Euphorbiaceae extracts have been reported for their capability to transform at most 10 of the immune parameters. Latex extract of *Euphorbia cotinifolia* and *E. tirucalli* effectively induces uniformly proliferation and apoptosis in PBMC. Subfraction of *E. tirucalli* was reported for its ability to induce lymphocyte proliferation by without accessory cells.

7.2. Analgesic

Analgesic potential of various extract of latex of *E. tirucalli* was performed by using tail immersion and acetic acid induces writhing techniques. Percentage inhibition of aqueous, dichloromethane-methanol and petroleum ether extracts was 57.67%, 51.80% and 48.48% respectively. Treatment at dosage 300 mg/kg of aqueous, 100 mg/kg of dichloromethane-methanol and 30 mg/kg of petroleum ether extracts extensively ($P < 0.01$) decreases the number of writhes [76].

7.3. Anthelmintics

A study on anthelmintic activity of petroleum ether and dichloromethane-methanol extract of latex of *E. tirucalli* has

Table 1
Physical constituents present in *E. tirucalli*.

Parameters		Values (%)	Refs
Quantitative standards	Foreign matter	Not more than 1%	[4]
	Ash	Not more than 12%	[4]
	Acid-insoluble ash	Not more than 2.5%	[4]
	Ethanol soluble extractive	Not less than 13%	[4]
	Water soluble extractive	Not less than 22%	[4]
Latex	Solid matter	28	[50]
	Caoutchouc	2.8–3.8	[7]
	Water soluble substances	53.8–79.9	[7]
	Resin soluble substances	59–63	[50]
	Rubber-like substances	12–14	[50]

Table 2
Chemical constituents present in different parts of *E. tirucalli*.

Plant part	Phytoconstituents	Refs
Latex	Triterpenes	[51,52]
Latex	Diterpene esters of phorbol, 12-deoxyphorbol esters and ingenol	[6]
Latex	β-sitosterol, euphorbol hexacosonate, 12-deoxy-4β-hydroxyphorbol-13-phenyl acetate-20-acetate, 12, 20-dideoxyphorbol-13-isobutyrate, glut-5-en-3-β-ol and euphol	[53,54]
Latex	4-deoxyphorbol di-ester	[55]
Latex	Cycloeuphordenol (triterpene)	[56]
Latex	Cyclotirucanenol (triterpene)	[57]
Latex	Diterpene ester	[54]
Latex	Highly irritant euphorbia factors (not specific)	[58]
Latex	Serine proteases	[59]
Latex	Euphol	[60,61]
Latex	Steroids	[62]
Latex	Tirucalicine (diterpene)	[57]
Latex	Tri-methyl ellagic acid	[63]
Fresh latex	Terpenic alcohol, isoeuphorol, taraxasterol and tirucallol	[6]
Undried latex	3,7,12-tri-O-acetyl-8-isovaleryl-ingol	[54]
Dried latex	Ketone euphorone and resin	[6]
Stem	Hentriacontene, 4-deoxyphorbol ester, hentriacontanol, β-sitosterotchouc, cyclotirucanenol, cycloeupordenol, corilagin, casuarin, euphorbins, euphorone, euphorcinol, euphol, gallic acids, ellagic acids and glucosides	[54]
Stem	Ellagic acid, taraxerol, 3,3′-di-O-methylellagic acid, β-sitosterol	[64]
Stem	Euphorbin A (polyphenol), euphorbin F (14) (dimers), tirucallin A (7) (tannin) and tirucallin B (11)	[65]
Bark	Euphorbol, β-sitosterol, cycloartenol, 24-methylenecycloartenol, ingenol triacetate, euphorbol hexacosonate, 12-deoxy-4β-hydroxyphorbol-13-phenyl acetate-20-acetate, taraxerone	[66]
Stem-bark	Cycloart-23-ene-3β,25-diol, euphorcinol	[67,68]
Stem-bark	Taraxerane triterpene	[69]
Stem-bark	Euphorginol	[70]
Stem-bark	Taraxerol	[71]
Fresh stem-bark	Euphoriginol, taraxer-14-en-6α-ol	[69]
Stem callus	Campesterol, stigmasterol, beta-sitosterol, isofucosterol, cycloartenol (sterols), euphol and beta-amyrin (triterpenoids)	[72]
Shoot callus	Sitosterol, stigmasterol, campesterol, palmitic acid and linoleic acid	[73]
Leaves	β-amyrin	[74]

been reported with ten unusual concentrations (0.1%–1.0%) against *Pheretima posthuma* earthworm. The entire test group's exhibits decrease in time period to paralysis and death of earthworm in petroleum ether and dichloromethane-methanol extracts [77].

7.4. Antiarthritic

The antiarthritic study of biopolymeric fraction (BET) of *E. tirucalli* was reported using adjuvant-induced arthritis model in rats by Sarang *et al.* [78]. BET treated animal shows dose dependent reduction in paw edema. Administration of dose of 400 mg/kg BET once daily up to 30 days did not show any noticeable unusual change or death.

7.5. Antibacterial/antifungal/antimicrobial

Antimicrobial effect of petroleum ether and dichloromethane-methanol extract of latex of *E. tirucalli* was performed using *Bacillus subtilis* (*B. subtilis*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*) by agar well diffusion assay. The aqueous extract was also tested against *Aspergillus niger* (*A. niger*), *Penicillium chrysogenum*, *Trichoderma viride* and *Candida albicans* (*C. albicans*) by agar well diffusion assay. Zone of reduction was determined for bacteria at 5%, 10%, 15% and 20% and for fungi at 3%, 6%, 9% and 12% concentrations. *B. subtilis* was resistant to tested extracts [77]. Antibacterial and antifungal effect of methanol, chloroform, n-hexane and aqueous extracts from *Sapindus emarginatus*, *Hibiscus rosa-sinensis*, *Mirabilis jalapa*, *E. tirucalli*, *Vitex negundo* and *Saussurea lappa* against *B. subtilis*, *Escherichia coli* (*E. coli*), *Staphylococcus epidermidis* bacterial strains and *Aspergillus flavus* (*A. flavus*), *C. albicans* and *Candida glabrata* fungal strains using agar diffusion and agar tube dilution assays. Result of these studies reports zone reduction by *n*-hexane extract of *E. tirucalli* at concentration 100 mg/mL [79]. Antimicrobial potential of acetone, chloroform, hexane, petroleum ether and methanol extracts of stem of *E. tirucalli* was performed using *Bacillus megaterium*, *B. subtilis*, *E. coli*, *Enterococcus faecalis*, *Proteus vulgaris* (*P. vulgaris*), *P. aeruginosa*, *S. aureus*, *A. niger*, *Aspergillus fumigatus* and *C. albicans*. Acetone extract is reported for inhibition in the direction of all micro-organisms. *E. coli* was found very sensitive to acetone extract. Chloroform extract was reported as an active extract against *B. subtilis*, *E. coli*, *P. vulgaris*, *S. aureus*, *A. niger* and *C. albicans*. Methanol extract was reported as an active extract against *B. subtilis*, *E. coli*, *Enterococcus faecalis*, *S. aureus* and *C. albicans*. Petroleum ether and hexane extract did not show any activity [80]. Antimicrobial potential of crude alcoholic extract of leaf and stem of *E. tirucalli* against the different microbial strains such as *E. coli*, *P. vulgaris*,

Salmonella enteritidis, *B. subtilis*, *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, *C. albicans*, *Candida tropicalis* (*C. tropicalis*), *A. niger*, *Aspergillus fumigatus*, *A. flavus* and *Fusarium oxysporum* by disc diffusion method has been reported. *E. coli* and *P. aeruginosa*, *K. pneumoniae* and *S. aureus* were responsive to leaf extract. Stem extract exhibit considerable antimicrobial potential in opposition to *P. vulgaris* and *K. pneumoniae* [81]. Antibacterial property of water and methanol extract of some medicinal plants has been evaluated by Parekh and Chanda, 2007 [82]. Antifungal effect of methanol extract of 90 Indian medicinal plants were tested using some yeasts *viz*., *C. albicans*, *Candida glabrata*, *C. tropicalis*, *Candida luteolus*, *Candida neoformans*, *Trichosporon beigelii* and molds like *Aspergillus candidus*, *A. flavus*, *A. niger* and *Mucor hiemalis* at 30 unusual concentration using agar disc diffusion assay by Parekh and Chanda, 2008. Results revealed that the antifungal effect was not concentration dependent. *A. flavus* was mainly inclined fungal strain and *Candida glabrata* was defiant [83]. Antimicrobial potential of methanolic, acetone, ethyl acetate, water and gemmomodified extract of *Terminalia arjuna* and *E. tirucalli* was evaluated by disc diffusion technique by Nazish *et al*., 2008. Bacterial strains *viz. B. subtilis*, *S. aureus*, *E. coli*, *Pasteurella multocida* and fungal strains *viz. Rhizoctonia solani* and *A. niger* were used. The methanolic extract of *E. tirucalli* was reported for maximum outcome against *S. aureus* and *B. subtilis* at 1000 μg concentration. Gemmomodified extract of *E. tirucalli* was more efficient in opposition to *E. coli* [84]. Antimicrobial potential of ethanolic extract of thirteen plants normally used in Governador Valadares peoples was checked using *S. aureus*, *Eclipta alba* (*E. alba*), *Arctium lappa*, *Cota tinctoria*, *Erigenia bulbosa* (*E. bulbosa*), *Mikania hirsutíssima*, *Solidago microglossa* (*S. microglossa*), *Silene dichotoma*, *Polygala glomerata*, *Santalum lanceolatum*, *Vernonia condensata* and *Lippia alba* by Beatriz, 2006 [85]. Results of these studies showed that antimicrobial potential in opposition to *S. aureus* and *E. alba* was > 1 mg/mL. The *A. lappa*, *C. tinctoria*, *E. bulbosa*, *Mikania hirsutíssima*, *S. microglossa*, *Silene dichotoma* was > 5 mg/mL and *Polygala glomerata*, *Santalum lanceolatum* and *Vernonia condensata* was > 10 mg/mL and *L. alba* was > 20 mg/mL. Extract did not show any activity in opposition to *E. coli*. Antibacterial and antifungal potential of toluene, ethyl acetate and methanol extract of eleven plants from different families were evaluated using agar well diffusion assay by Chanda and Bharavalia. Two gram +ve bacteria such as *S. aureus* and *B. subtilis* and gram −ve bacteria like *P. aeruginosa* and *E. coli* and four fungi viz. *C. albicans*, *C. tropicalis*, *C. neoformans* and *Cryptococcus luteolus* were used in the experiments. All extracts were exhibited changeable scale of antibacterial and antifungal potentials [86]. Antimicrobial potential of methanol extract of eleven plants against eight micro-organisms by agar well diffusion method was investigated. The methanol extract have showed highest activity with gram +ve bacteria and fungi. *E. tirucalli* have shown best antimicrobial activity [87].

7.6. Anti-HIV

Anti-HIV screening of the crude alcoholic extract of leaf and stem of *E. tirucalli* was carried out using HIV protease colorimetric assay and has been reported as effective anti-HIV activity [81].

7.7. Anti-inflammatory

Anti-inflammatory effect of euphol was checked by carrageenan-induced mechanical hyperalgesia at 30 and 100 mg/kg dose levels. The keratinocyte derived chemokine, IL-1b, IL-6 and tumor necrosis-α factor related to inhibition of myeloperoxidase action were considered for further evaluation. Therefore, the outcome was substantiated to facilitate the euphol for managing inflammatory conditions [61]. Anti-inflammatory activity of petroleum ether, dichloromethane-methanol and aqueous extract of latex of *E. tirucalli* were evaluated by carrageenan-induced paw edema by Prabha *et al*., 2008. Ibuprofen was considered as standard drug. Results of the present study revealed that petroleum ether, dichloromethane-methanol and aqueous extract showed considerably ($P < 0.01$) inhibition of inflammatory edema in rats at dosages 30, 100 and 300 mg/kg extracts, respectively [76].

7.8. Antioxidant

Antioxidant study of methanol extract of eleven plants was investigated by DPPH, superoxide, hydroxyl radical, reducing capacity. Methanol extract of all the plants was exhibited potent antioxidant action [87]. Antioxidant effect of aqueous extract of *E. tirucalli* has been studied using reducing capacity, superoxide anion and hydroxyl radical scavenging assay [88]. Hepatic damage was induced by CCl_4. Aqueous extract have shown dosage dependent antioxidant effect. Proteins were extracted from the laticifer cells of 30 plants. They have been examined for antioxidant potential using colorimetric methods. Acidic proteins have molecular masses of 12.5 and 74.5 kDa predominate in laticifers of *Plumeria rubra* while *Conradina grandiflora* and *E. tirucalli* did not possess [89].

7.9. Antiviral

Antiviral potential of petroleum ether and dichloromethane-methanol extract of *E. tirucalli* latex was investigated using tobamo viruses such as tobacco and tomato mosaic viruses by Ramesh *et al*. [90]. A concentration of extracts at 50, 100 and 150 ppm of was used. Petroleum ether extract have showed 80% defense in opposition to tomato mosaic virus at 150 ppm. The dichloromethane-methanol extract have showed 81% defense against tobacco mosaic virus at 150 ppm. Lytic effect of herpes simplex virus type-2 was performed by end-point titration technique. The water and methanol extract of *Euphorbia cotinifolia* and *E. tirucalli* was establishing maximum action [91].

7.10. Biodiesel production

E. tirucalli contains a good amount of terpenoids which are efficient to produce biodiesel from the plant. This biodiesel is a non-toxic and environment friendly. It is producing less carbon monoxide and sulfur dioxide emissions. Hence, it is best fuel for greatly contaminated cities [92].

7.11. CNS depressant/neuropathic pain

Euphol has been tested for preventing neuropathic pain induces by ligation of sciatic nerve. The pretreatment among CB1R and CB2R antagonist and knock-down gene of CB1R and

CB2R appreciably inverted anti-nociceptive action of euphol. A result reveals that euphol was a promising entity for managing the neuropathic condition [61]. CNS depressant effect of petroleum ether, dichloromethane-methanol and aqueous extract of *E. tirucalli* latex was evaluated by locomotor behavior using actophotometer. Chlorpromazine was used as a standard reference drug. Locomotor behavior score was more appreciably decreased in aqueous extract next to dichloromethane-methanol and petroleum ether. These effects of extracts are possibly due to augment in the concentration of GABA in the brain [93].

7.12. Cytotoxicity/anticancer

Anticancer activity of euphol was studied using human gastric cancer cells. Elevated cytotoxicity was shown by euphol in human gastric CS12 cancer cells than non-cancer CSN cells. Anti-proliferative effect of euphol was due to the improved $p27^{kip1}$ and decreasing cyclin B1 levels. The inhibitions of ERK1/2 activation through PD98059 upturned euphol induce pro-apoptotic protein expression and cell death. Therefore, euphol selectively induces apoptosis of gastric cancer cells by means of modulation of ERK signaling which might be useful in cancer treatment [60]. Medicinal plants used by Governador Valadares peoples were evaluated using BST assay by Beatriz *et al*. [85]. Ethanol extracts of ten plants viz., *Cymbopogon nardus*, *Calpurnia pisonis*, *E. bulbosa*, *E. alba*, *E. tirucalli*, *Eryngium foetidum*, *Momordica charantia*, *Millettia hirsutissima*, *Panulirus ornatus* and *S. microglossa* were showed LD_{50} < 1000 ppm. Forty-seven plant extracts together with *E. tirucalli* were tested for their anti-proliferative and cytotoxic potential by MTT assay [91]. Cytotoxic actions of *Euphorbia fischeriana*, *E. tirucalli*, *Egletes humifusa* and *Euphorbia antiquorum* extracts were evaluated using BEL-7402 (*Hepatocyte carcinoma*) and A-549 (Lung carcinoma) cell-lines. Chloroform extract of *Euphorbia antiquorum* and *E. tirucalli* showed good cytotoxic actions [94]. Cytotoxic and apoptotic effect of crude milky juice of *E. tirucalli* on human cancer cells were performed by Abul-fetouh *et al.* [95]. Glioma, myelogenous leukemia and breast cancer cells were used in the study. The methotrexate sodium was considered as reference drug. Malignant cells have shown treatment with sap and time dependent method and IC_{50} of crude juice was found 10 μL. Cell cycle study indicated crude juice as a proficient for arresting maximum cells in G1 phase. Twenty one plants were used in Tabora region of Western Tanzania for cancer conditions. Therefore, ethanol extracts of plants was showed low, intermediate and high toxicity [96]. Homeopathic medicine from *E. tirucalli* was prepared by mother-tincture according to centesimal Hahnemannian technique. 0.5% and 5% of 70° GL solutions of ethyl alcohol were prepared. However, the treatment by 0.5% solution of *E. tirucalli* 30 cH was showed 32.1% reduction of cell proliferation [97]. Physical and chemical characters of LM preparations on biological methods were performed using MTT assay by Sheila *et al*. [98]. Cytotoxic effects of high dilution of latex against MelanA (Non-tumoral melanocytes) and MCF-7 (Breast Carcinoma) cell lines were studied using MTT and May-Grunwald-Giemsa assays. Ultra-structure of cell was analyzed using transmission electron microscopy. Enzyme 6-phosphofructo-1-kinase (PFK-1) activity was studied by spectrophotometric assay. Aveloz 15 cH was showed increased in viability of MCF-7 cell line [99]. Ethanol extract of stem bark of *E. tirucalli* was studied for its inhibitory activity by Patil and Mugdum where it showed effective inhibition [100]. Colitis was induce using dextran sulfate sodium and 2,4,6-trinitrobenzene sulfonic acid. Effect of euphol was assessed by proinflammatory mediators and cytokines through immunohistochemistry, ELISA, RT-PCR and flow cytometry. Euphol showed considerable decrease in colitis, histological damage score and myeloperoxidase activity in colonic tissue. It also showed decrease in IL-1b, MCP-1, MIP-2, TNF-a and IL-6 levels and reduction of expression of NOS2, VEGF and Ki67 [101].

7.13. Genotoxic/mutagenic

Aveloz latex and phytotherapic solutions were prepared from *E. tirucalli* and evaluated for their genotoxic and mutagenic effect by induc, ames and chromo test. A result of induc test was showed no decrease in bacterial survival and increase in lysogenic cycle. Ames and chromo test did not show mutagenic or genotoxic effects [102].

7.14. Hepatoprotective

Aqueous extract of *E. tirucalli* was tested against CCl_4 induced hepatic damage in rats by Jyothi *et al.* [88]. The extract was produced considerable hepatoprotective activity by decrease in levels of serum bilirubin, cholesterol, triglycerides and tissue lipid peroxidation. GSH level in tissue was increased.

7.15. Insect repellants

The insect repellant activity of five plant species was examined by Coleoptera pests [103]. Latex of *E. tirucalli* was showed deterrent activity.

7.16. Immunomodulatory

Immunomodulatory study of biopolymeric fraction (BET) of *E. tirucalli* was evaluated for delayed type hypersensitivity, leukocyte migration, vascular permeability, lymphocyte immunophenotyping and IL-2 and IFN-γ [78]. BET significantly decreases 25.0%–28.2% DTH response, dose dependent reduction of total leucocytes count and vascular permeability. Production of TNF-α, IFN-γ and IL-4, IL-10 cytokines were evaluated using crude latex of *E. tirucalli*. Result showed significant increase in percentage of $CD4^+$ T lymphocytes which was positive for TNF-α, IFN-γ and IL-10 [104].

7.17. Larvicidal

Larvicidal effect of petroleum ether, ethyl acetate and butanol extract of *Jatropha curcas*, *Pedilanthus tithymaloides*, *Phyllanthus amarus*, *Euphorbia hirta* and *E. tirucalli* were studied using 4th instar larvae of *Aedes aegypti* and *Culex quinquefasciatus*. Low larvicidal effects were showed by the extracts [40]. Larvicidal efficiency of *E. tirucalli* latex was studied using *Anopheles fenestus* and *Anopheles gambae* Giles by Mwine *et al*. [105]. Latex showed total mortality with highest dilution 1: 250 at 5 days. LT-50 and 90 was 12 and 36 h for same dilution.

7.18. Molluscicidal/ovicidal/piscicidal

Molluscicidal and ovicidal potential of euphorginol isolated from stem bark of *E. tirucalli* using *Lymnaea acuminata* (*L. acuminata*) and *Indoplanorbis exustus* snails. Euphorginol was shown considerable negative relationship among LC value and disclosure periods. Therefore, the LC_{50} value of euphorginol was decreased against both snails [70]. Taraxerol and acetone extract of *E. tirucalli* was studied using *L. acuminata* snail for molluscicidal efficacy. *E. tirucalli* acts as a prospective resource of molluscicides [71]. Effect of aqueous extract of latex of *E. tirucalli* was studied using snail *L. acuminata*. Results showed considerable changes in pyruvate, glycogen, total protein, lactate and free amino acid levels with an enzyme succinic dehydrogenase, protease, cytochrome oxidase, alanine aminotransaminase and aspartate found in nervous, hepato-pancreatic and ovotestis tissues of fresh water vector snail [106]. Effect of powder of latex and stem-bark of *E. tirucalli* was performed using fresh water snail *L. acuminata* Lamarack and *Indoplanorbs exustus*. *E. tirucalli* extract showed significant inhibition of enzyme acetylcholinesterase [107]. Piscicidal potential of aqueous extract of stem-bark and latex of *E. tirucalli* was reported by Tiwari and Singh [42]. Extracts appreciably ($P < 0.05$) alters the level of total free amino acids, total protein, glycogen, nucleic acids, lactate, pyruvate, protease, alanine and acetylcholinesterase, aspartate aminotransferase and cytochrome oxidase enzyme activities in *Channa punctatus* fresh water fish. Acute toxicity of aqueous extract of *E. tirucalli* latex was evaluated using *Heteropneustes fossilis* fresh water fish. *E. tirucalli* showed higher piscicidal effect when compared with another synthetic pesticide [108].

7.19. Myelopoiesis

Myelosuppression effect was studied by increased number of spleen CFU-GM in tumor-bearing mice. *E. tirucalli* extract were stimulated narrow myelopoiesis and reduced spleen colony formation in treated animals. Therefore, the extract was appreciably improved survival and reduced tumor growth [109].

7.20. Proteolytic/chitinolytics

Proteins were extracted from laticifer cells of *Plumeria rubra*, *Conradina grandiflora* and *E. tirucalli* and examined in respect of proteolytic and chitinolytic effects by zymography and colorimetric assays. The acidic proteins were not predominated in laticifers of *E. tirucalli* while chitinase action was predominated [89].

7.21. Tumor promoter activity

E. tirucalli unpurified latex was studied for Epstein–Barr virus gene expression. Different dilutions of latex were used as a treatment in Burkitt lymphoma cell line. It was reported that latex was able to reactivate the Epstein–Barr virus lytic cycle in a dose dependent mode. Latex treated with protein kinase C inhibitor was blocked cycle activation [110].

8. Toxicity studies

The developmental toxicity of aqueous solution of *E. tirucalli* latex was studied by Aldo Cesar *et al*. *E. tirucalli* did not obstruct tubaric embryo growth or implantation. It also alters the placenta morphology [111]. Effects of latex of *E. tirucalli* were evaluated by Marcia *et al*. The animals showed a considerable ($P < 0.05$) increase in food consumption without weight gain [112].

9. Conclusions

As per the literatures, most of the pharmacological activities were performed on latex of *E. tirucalli* by *in-vitro* and *in-vivo* experimental techniques. However, there is a need to explore molecular mechanisms for all the reported activities of *E. tirucalli*. There is lacking of isolation, structural elucidation and confirmation many more phytoconstituents by sophisticated instrumental analysis techniques from the plant. Exploration of toxicity of reported phytoconstituents is yet to be performed. *E. tirucalli* is not mentioned in Ayurvedic Pharmacopeia of India, it should be incorporated. Therefore, this plant can also be incorporated into the syllabus of undergraduate and postgraduate botany, Ayurveda and pharmacy courses. There are very few patents on *E. tirucalli* were reported so far.

Conflict of interest statement

Authors declare that they have no conflict of interest.

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