ISSN: 2322 - 0902 (P)
ISSN: 2322 - 0910 (O)

International Journal of Ayurveda and Pharma Research

Review Article

A REVIEW ON THERAPEUTIC AND PHARMACOGNOSTIC PROPERTIES OF *VELLARUGU* (*ENICOSTEMMA LITTORALE* BLUME)

Vinotha Sanmugarajah
Senior Lecturer, Unit of Siddha Medicine, University of Jaffna, Sri Lanka.

ABSTRACT

Vellarugu {*Enicostemma littorale* Blume (*E. littorale*)} (Gentian family) is a highly nutritious perennial medicinal plant and used as a medicine in Siddha Medical System to treat several disease conditions such as diabetes mellitus, rheumatism (*Vata* diseases), skin diseases (*Pitta* diseases), constipation, abdominal ulcers, swelling, obesity and insect poisoning. It is a rainy season herb, growing on moist, damp and shady ridges and slopes of the borders of cultivated fields and widely distributed in India, Eastern and Southern Africa, South America, and Asia. Whole plant, Leaves, Flowers, stem and Roots are mostly used for the treatment. Although there are numerous scientific studies related to multiple usage of *Vellarugu* plant, this study attempts to collect all available information and prepare a monograph about the *E. littorale* for documentation purpose. *E. littorale* has a number of anti-oxidative phytochemicals which include five alkaloids, catechins, saponins, two sterols, triterpinoids, phenolic acid, flavonoids, xanthones and volatile oil, swetiamerin, and gentianine. Higher percentage of total ash, water soluble ash and acid insoluble ash also were found in this plant. *E. littorale* has very low toxicity and is a safe and the presence of heavy metals was below the WHO/FDA permissible limits. Numerous studies stated that E. littorale has the therapeutic pharmacological actions such as anti-diabetic, antioxidant, hypolipidaemic, hepatoprotective, anti-inflammatory, analgesic, anti-arthritic, anti-microbial, anti tumour, and etc. This monograph may provide and confirmed the documentary evident for multiple medicinal and therapeutic uses and pharmacological effects of the *E. littorale*.

KEYWORDS: *Vellarugu*, *Enicostemma littorale*, Pharmacognosy, Therapeutic Uses.

INTRODUCTION

Two systems of Medicine namely Allopathic and Indigenous are mainly practiced in Sri Lanka. In all, the three indigenous systems (Ayurveda, Siddha and Unani Medicine) in Sri Lanka, different parts of the medicinal plants play a major role and constitute the backbone of the system. Siddha Medicine is one of the traditional medicine and popular among the Tamil speaking people of Northern and Eastern Provinces of Sri Lanka.

Medicinal plants have been playing an essential role in the development of human culture. As a source of medicine, Medicinal plants have always been at forefront virtually all cultures of civilizations.[1] Medicinal herbs have been known for centuries and are highly valued all over the world as a rich source of therapeutic agents for prevention of diseases and ailments.[2] Even today, the World Health Organization (WHO) estimates that up to 80 percent of the world population still relies mainly on traditional remedies such as herbs for their primary health care.[3] Ahmed et al., (2004) mentioned that according to a survey conducted by W.H.O., traditional healers treat 65% patients in Sri Lanka and 80% in India.[4]

Approximately 72,000 plant species were estimated for having medicinal properties. Of which, India recognizes 3,000 plant species for having medicinal values.[5] The WHO has appreciated the importance of medicinal plants for public health care in developing nations and has evolved guidelines to support the member states in their efforts to formulate national policies on traditional medicine, and to study their potential usefulness including evaluation, safety, and efficacy.[6]

Vellarugu {*Enicostemma littorale* Blume (*E. littorale*) (*Enicostemma hyssopifolium*)}[7] plays a vital role in human healthcare.[5] *E. littorale* (Gentian family) is an herbaceous plant and seem to be rich in medicinal compounds.[8] It is a well-known plant used as drug in Ayurveda, Unani, Siddha, Allopathic, Homeopathy, Naturopathy and Home Remedies[9] and it is widely used in Siddha system of medicine under the name "*Vellarugu*".[10-12] It is commonly known as Chota-kirayata or Chotachiryata

(Hindi) and Mamejava (Gujarati)[13] has been widely used in traditional system of medicines for the treatment of diabetes mellitus, arthritis, rheumatism, constipation, abdominal ulcers, hernia, swelling, fever, skin diseases and insect poisoning.[14-16] It is also one of the herbs widely used for treating and alleviating the effects of both type I and II diabetes.[17]

The present study objective is based mainly review on the therapeutic and pharmacognostic research work of *E. littorale*. This systematic monograph contained information's represents a review of the authoritative scientific and traditional data. All efforts have been done to assure the accuracy of the information and findings were presented.

Scientific Classification [5,18]

Kingdom:	*Plantae*
Subdivision:	*Angiospermae*
Class:	*Dicotyledonae*
Subclass:	*Gamopetalae*
Serius:	*Bicarpellatae*
Order:	*Gentianales*
Family:	*Gentianaceae* (Gentian family)
Genus:	*Enicostemma*
Species:	*littorale*

Taxonomic Position [19-24]

Nomenclature: The word Enicostemma is probably formed from the three words, "en" means inside, "icos" means 20 and "stemma" means wreath or circle due to the many flowers arranged in circles in the leaf axils along the stem.[5]

Botanical name	*Enicostemma littorale,* Blume
Synonyms	*Enicostemma axillare* (Lam.) Raynal *Adenema hissopifolia* *Enicostemma hyssopifolium* (willd) –Verdooram

Vernacular names

Common name:	Chota-kirayata
Tamil name:	*Vellarugu, Vallari*, *Arukumuli, Chakkiraviraiyantan*
English name:	Indian gentian, White head
Sanskrit name:	*Krimihrita, Magajihva, Mamajaka, Nagajiuha*
Ayurvedic name:	*Naagjhvaa, Maamajjaka, Naahi, Maja-makkabooti, Tiksh-napatraa, Mamejav, Chhotaa Chirayataa*
Unani name:	*Naai, Naahi*
Hindi:	*Chota-kirayat*or, *Chotachirayata*
Bombay:	*Kada-vinayi, Manucha*
Bengali:	*Nagajivha*
Malayalam:	*Vallari, Vellarugu*
Kannada:	*Enicostemma*
Telugu:	*Nella-galli, Nela-guli, Chevvu-kurti*
Gujarati:	*Mamejava*
Marathi:	*Chotachirayita, kadavinayi*
Additional names:	*Gormadi koora* (In the UK product description for Glucostat, Maharishi Ayurveda Products (2006), incorrectly refers to *E. littorale* as Indian Gentian

Geographical Distribution

This tropical genus is widely distributed in many parts of India such as Punjab, Bombay, except in Bengal, Eastern and Southern Africa, South America, and Asia.[14, 15, 19, 25] In Sri Lanka, it is found in on open, sandy places among sparse grass close the beach throughout the dry zone particularly from northwestern to northeastern coastal belt.[25] It is a rainy season herb, growing on moist, damp and shady ridges and slopes of the borders of cultivated fields.[19, 26] *E. littorale* grows in many diverse habitats from savannas, grasslands, forests to beaches, from wet to very dry and also survives in a very saline environment.[5]

Distribution is throughout India in areas up to 450 m elevation, common coastal areas among grasses. When growing in good soil, away from the sea this plant attains larger size with large broad leaves than the one near the sea.[9, 27]

Flowering and Fruiting season: From July to November.[27]

Collection: October-November

Parts Used

Whole plant, Leaves, Flowers, stem and Roots are mostly used for the treatment.[10, 12, 15]

Botanical Description[10, 12, 15, 21, 28]

It is an erect, perennial herb attaining height of 15-20 inch, simple or branched at the base (Figure: 1). Stem cylindric, glabrous with a decurrent ridge below each leaf, internodes short 0.8 to 1.5 cm long.

Leaves are opposite decussate, lanceolate, 3 to 6 by 0.5 to 0.7 cm, sessile, often narrow, green in colour, apex obtuse, 3 nerved, venation pinnate, upper surface rough, lower glabrous. Inflorescence in many flowered auxiliary clusters, numerous in the axils of each pair of leaves. Flowers are small white with green lines, drying yellowish, sessile or subsessile; white with green lines, drying yellowish, sessile or subsessile; whorled and in clusters, 5-merous (rarely 3-, 4-, or 6- merous); calyx narrow, 3 to 4 mm long, campanulate; divided down halfway to 2/3, thin, persistent in fruit, with colleters. Corolla small, white, 6 to 8 mm long, tubular to funnel shaped at the base contains numerous seeds. Ovary is without nectary disk; stigmas capitate, slightly bilobed. Fruit a capsule, obovoid, seeds rounded, not winged.

Root is slender, tapering, rough, secondary root filiform, 5 to 15 cm length, 0.3 to 2.5 cm in

diameter, light yellow externally, creamish white internally. Stamens inserted below the sinuses, just above the middle of the tube; filaments 1.5–2.3 mm long, with a double hood at the insertion point.

Figure 1: (a) complete plant (b) leaves and (c) Flowers of *E. littorale*

Microscopic Characters [9]

Dermal characters

Epidermal cells of adaxial epidermis are mostly with anisocytic stomata. Occasionally anomocytic stomata are also present; Epidermal cell with wavy margins. Cells are elongated at the coastal region. Epidermal cells of the abaxial epidermis are mostly elongated and straightwalled at the coastal region. Most dominant type of stomata on abaxial surface is anisocytic (Figure 2: A).

Occasionally diacytic and anomocytic stomatas are also seen. Epidermal cell with spongy wavy walls (Figure 2: A, B). Epidermis also shows non-glandular, multicellular trichomes having a single basal cell.

Transverse section of leaf of *E. littorale*[9]

The epidermis unilayered on upper and lower epidermis with thick cuticle, cuticle strianted hence appearing lobed in cut section at the midrib, there is a single layered hypodermis at an abaxial side. Mesophyll is made up of compact chlorenchyma. A vascular bundle is present inelement is facing upwards. The mesophyll of lamina is differentiated into two layered palisade towards the abaxial epidermis and 3-5 layered spongy chlorenchyma. Epidermis is studded with nonglandular epidermal trichomes. The trichomes are multicellular having a single basal cell (Figure 2: C).

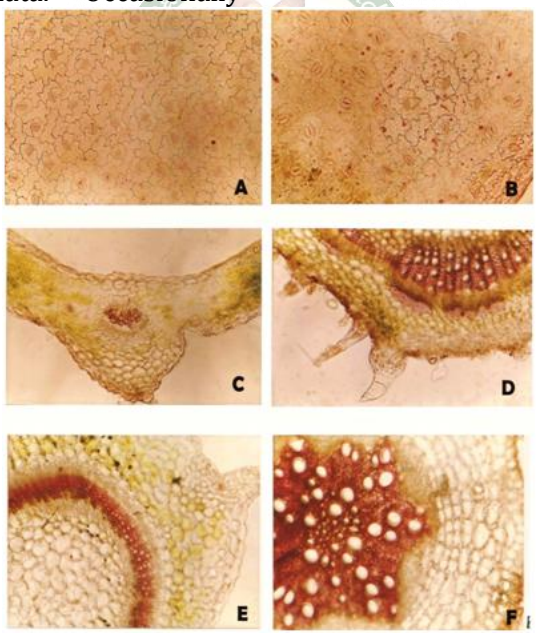


Figure 2: Anatomical features of *Enicostemma littorale* Blume

A: abaxial surface of leaf showing diacyticstomata and epidermal cells; B: abaxial surface of leaf showing diacytic stomata; C: T.S. of leaf; D: T.S. of petiole; E: T.S. of stem; F: T.S. of root

Transverse section of petiole stem of *Enicostemma littorale*[9]

The transverse section of the stem shows hexangular in outline, angles extending into a multicellular wing like structure. Epidermis with thick cuticle, unilayered small cells compactly arranged; following the epidermis is a thick cortex 6-15 layered which is parencymatous with scattered chlorenchymatus cell. Cortex is in wing 2-5 of compact Parenchyma. Stele consisting of band of xylem disrupted at poles. Polar xylem is lax, phloem is present in the form of continues band on both sides of xylem band. Sphaeraphides are occasionally seen in pith cells. Central pith is present (Figure 2: E).

Transverse section of root of *Enicostemma littorale*[9]

The transverse section shows circular in outline. Epidermis single layered, cortex 7-10 layered Epidermis single layered, cortex 7-10 layered parenchymatous, stele consisting of star shaped and xylemis surrounded by phloem zone. Vessels are embedded with thick-walled xylem sclerenchyma. Pith obscure (Figure 2: F).

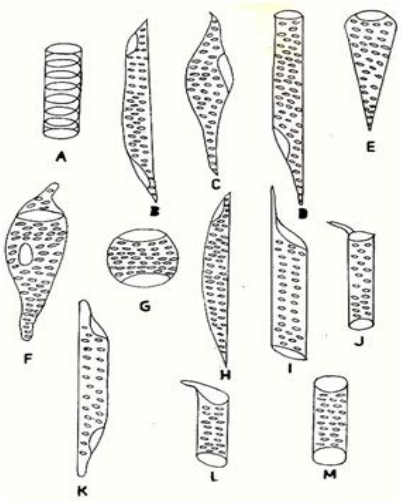


Figure 3: Vessel elements (VE) of *Enicostemma littorale* Blume

A: Cylindrical VE with spiral thickening; B, H: Linear VE with irregular pitted thickening; C: Spiral VE with irregular pitted thickening; D: Wedge shaped VE with irregular pitted thickening; E: Top Shaped VE with irregular pitted thickening; F: Fusiform VE with irregular pitted; G: Oblong VE with irregular pitted thickening; I: VE with long pointed tail; J: VE with long blunt tail; K: VE with Short blunt tail; L: VE with transverse end wall; M: VE with oblique end wall.

Siddha And Ayurvedic Properties[14]

Suvai/ Rasa (Taste): *Kaippu/ Tikta* (Bitter)

Veeriyam (Potency): *Veppa/ Ushna* (Hot)

Vipakam (Efficacy): *Kaarppu/ Katu* (Pungent)

Form of Medicine: Decoction, *Chooranam* (Powder medicine), and *Patpam* (fine powder). [10, 12]

Standard Dosage

Powder: 2.5 – 5 g daily[20]
1 – 3 g [21]

Decoction: 50 – 100 ml [20, 21]

Figure 4: Shade dried plants of *E. littorale*

Figure 5: Whole plant powder of *E. littorale*

Traditional Uses

Decoction, *Chooranam* and *Patpam* of *E. littorale* are used for Diabetes mellitus, control arthritis, rheumatism, hernia, constipation, abdominal ulcers, *Vata* diseases swelling, and itching, insect poisoning.[5,10,12,14,15] The decoctions attained from the *E. littorale* leaves are used in rheumatism, abdominal ulcers, hernia, swelling, itches and insect poisoning.[29]

Dried powdered (Figure:5) with honey is used for blood purifier and in dropsy, rheumatism, itches, inflammatory conditions, swelling.[18, 23], [30, 31]

E. littorale Paste is locally applied in snake bite[32] and on boils.[23] *E. littorale* is pungent and very bitter used for anthelmintic and reduces fever and in as stomachic. The plant is crushed and applied locally in snack-bite and also acrid thermogenic, digestive, tonic, carminative, laxative, anti-inflammatory, urinary astringent, depurative, repulsive and anti-periodic and useful in dyspepsia, colic flatulence, abdominal ulcers, hernia, constipation, dropsy swellings, vitiated conditions of *Kapha* and *Vata*, hepathopathy, glycosuria, leprosy, skin diseases, prutitus, intermittent, fever and malaise.[9]

Mishra et al., stated their review article in 2017 that the bitterly natured *E. littorale* acts as a laxative, helps in curing fever, rheumatism, skin diseases, abdominal disorders, snake bite, obesity and helps to regulate blood sugar levels.[33]

Nutritional Information of *E. Littorale*

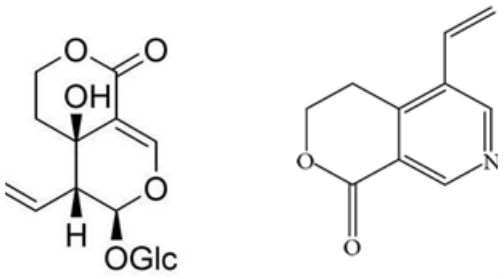
The nutritional analysis report of Indian Council of Medical Research suggests that 100 g of fresh *E. littorale* greens contains 140 kcal energy, 7 g of protein, 0.7 g of fat, 26.5 g of carbohydrate, 4.2 g of fiber, 8.4 g of minerals, 49.9 mg of iron, 1.641 mg of calcium, 81 mg of phosphorous.[5], [34, 35] Daily intake of 2 g of *E. littorale* fresh leaves is recommended for diabetic patients since it's highly nutritious.[36]

Chemical Constituents

E. littorale contains phytochemicals are swetiamerin, vanilic acid, ferulic acid, pcoumaric acid apigenin, genkwanin, isovitexin, swertisin, seponarin, gentiocrucine, and enicoflavine.[37] It has a number of anti-oxidative phytochemicals which include five alkaloids, catechins, saponins, two sterols,

triterpinoids, phenolic acid, flavonoids, xanthones and volatile oil.[13, 18] Gentianine is a bitter, crystalline; monoterpene alkaloids like enicoflavin and gentiocrucine were isolated.[13], [38, 39]

Ambikapathy et al., have found in 2011 that the GC-MS analysis of *E. littorale* whole plant methanol extract revealed the existence of the ether compound-Laminaribiitol (79.93%), 12-hydroxy-9-octadecenoic acid (9.546%), Myricetin (4.7519%), 3.3-Methylenebis (4- hydroxycoumarin) (2.811%) and catechin (2.002%).[40] Further, *E. littorale* has isolated betulin, a triterpenesapogenin, a bitter glycoside, ophelic acid, alkaloids, gentianin, a secoiridoid glycoside, swertiamarin, phytosterol, sugars and tannins.[20, 31, 41]



a.Swertimarin ***b. Gentianine***

Figure 6: Structure of *Swertimarin* (a) Gentianine (b) of *E. littorale*

A new flavone C-glucoside named as Verticilliside was isolated. Steroids and triterpenoids (Enicoflavin and gentiocrucine, catechinsm, saponins, betulin, triterpene, sapogenin and sweriamarin), Flavonoids and xanthones (Apigenin, genkwanin, isovitexin, swerisin, saponarin, 5-O-glucosylswertisin and 5-Oglucosuliso swertisin), Phenolic acids (Vanillic acid, Syringic acid, p-hydroxy benzoic acid, protocatechuicacud, p-coumaric acid and ferulicacid), Aminoacids (L-glutamic acid, trytophane, alanine, serine, aspartic acid, L-proline, L-tyrosine, threonine, phenyl alanine, L-histidinemonohydrochloride, methionine, iso-leucine, L-arginine monohydro chloride, DOPA, L-glycine, 2-amino butyric acid and valine).[5, 18, 42]

Praveena et al., 2014 have found that the Gas-chromatogram and mass spectral studies showed major chemical compounds in methanol fraction of *E. littorale* are 2-methoxy vinyl phenol (4.3649%), 4H-Pyran-4-one, 2, 3-dihydro-3, 5-dihydroxy-6-methyl (4.7692%), 1, 6-Anhydro-a-D glucopyranose (laevoglucose) (28.4683%), m-Toluic acid, allyl ester (8.8620%), Erythrocentaurin (7.9776%), and 2H-Pyran-2-one, 5, 6-dihydro-4- (2-methyl-2-propen-3yl) (10.6197%).[43]

Macroscopic and Organoleptic Properties of the Whole Plant Powder of the *E. Littorale*

Vinotha et al., found in 2014 that, the organoleptic characters of the *Vellarugu chooranam* (Whole plant powder of the *E. littorale*) were light greenish brown smooth fine powder with characteristic odour and high bitter taste. Its ethanol, methanol and aqueous extracts had similar organoleptic characters except the colour.[44]

Fluorescence analysis of the Whole Plant powder of the *E. Littorale*

Vinotha et al., 2014 and Vinotha 2015 have observed that, the colour of the extractsof *Vellarugu chooranam* (whole plant powder of the *E. littorale*) from organic and inorganic solvents were observed both under ordinary and UV light (Table 1) and there was little differencebetween extracts and the light sources.[44,45] Further mentioned that, these results was fairly comparable with those reported from previous study of fluorescence analysis of *E. littorale* done by *Kala et al.,* 2011.[46]

Table 1: Powder fluorescence analysis of *Vellarugu chooranam*

Vellarugu chooranam	**UV 254 nm**	**UV 366 nm**	**In day light**
Dry powder	Greenish brown	Greenish brown	Greenish brown
Powder (P) as such NaOH (1N) in water	Green	Dark green	Yellowish green
P + HCl (1N)	Green	Brown	Yellowish green
P + NaOH (1N) in MeOH	Green	Dark green	Yellowish green
P + 50% KOH	Light brown	Dark green	Yellowish green
P + H_2SO_4	Green	Dark green	Yellowish green
P + 50% HNO_3	Brown	Dark green	Yellowish green
P + concentrated HNO_3	Yellowish green	Dark Green	Brownish orange
P + CH_3COOH	Green	Dark green	Yellowish green
P + concentrated H_2SO_4	Dark brown	Dark green	Green
P + iodine in water	Dark brown	Dark brown	Yellow

Physico - Phytochemical Properties of *E. Littorale*

Qualitative analysis of the whole plant powder revealed the presence of minerals like iron, potassium, sodium, calcium, magnesium, silica, phosphate, chloride, sulphate and carbonate.[42, 47] Anwar et al., have found in 1996 that the A secoiridoid glycoside, swertiamarin, was isolated and

identified on the basis of UV, IR, Mass and NMR spectroscopic measurements from *E. littorale*.[48]

Vishwakarma et al., 2010 have reported that the aqueous extract of *E. littorale* showed the presence of triterpenoids, flavonoids, alkaloids and coumarins.[13] Vidyadhar et al., 2010 have found that the preliminary phytochemical screening has shown the presence of alkaloids, tannins, flavonoids, triterpenes and reducing sugars.[16] Subasini *et al*., have investigated in 2010 that the different extracts for phytochemical screening showed the presence of flavonoids, polyphenols, phytosterol, tannin, carbohydrate, amino acid, protein and vitamins like Vitamin C and E in 85% methanol; flavonoids, polyphenols and phytosterol in ethyl acetate; alkaloids andphytostero in hexane and chloroform extracts of *E. littorale*. [49] Gite et al. 2010 have found that the percent yields of petroleum ether, chloroform, methanol and water extractable matters were found to be 2.30, 3.10, 14.6 and 26.12% in whole plant of *E. littorale*. The physicochemical parameters total ash, acid insoluble ash and water soluble ash value were found to be 9.0, 8.75 and 7.28% respectively. The loss on drying and moisture content were found to be 6.68 and 4.26%; the phytochemical screening revealed that the presence of tannins, phenols, protein, amino acids, saponins, carbohydrates and flavonoids in aqueous and methanol extracts; steroids, protein, amino acids, fat and oils in petroleum ether extract and alkaloids, steroids, fat and oils in chloroform extract of *E. littorale*.[50]

A review article stated that *E. littorale* is a plant with a number of antioxidative phytochemicals, which include alkaloids, catechins, saponins, sterols, triterpenoids, phenolic acids, flavonoids and xanthone and also contains minerals like iron, potassium, sodium, calcium, magnesium, silica, phosphate, chloride, sulphate and carbonate.[18] Kala et al. (2011) have found that the higher percentage of total ash, water soluble ash and acid insoluble ash were found viz., 11.4, 4.26 and 2.10% respectively. Benzene, petroleum ether, chloroform, acetone, methanol, ethanol and water extractable matters were found viz., 12.31, 10.20, 9.48, 8.30, 11.36, 13.21 and 12.78% respectively. Preliminary phytochemical screening showed the presence of terpenoides, tannins, phenols, coumarin, flavonoids, protein and sugar in methanol extract; phenols, coumarins, flavonoids, tannins, saponins, sugar and anthraquinones in chloroform extract and terpenoides, coumarins, protein, tannins, saponins, sugar and anthraquinones in benzene extract of *E. littorale*.[46]

Hariram et al., 2011 have stated that the leaf and root of *E. littorale* showed maximum quantity of specific constituents when compare to the whole plant screening and the acetone extract showed glycosides, reducing sugars and terpenoids are seen in maximum and cardiac glycosides, steroids, alkaloids, flavonoids and tannin are present in traces in the whole plant compared with other plant parts of *E. littorale*.[51] Pandya *et al*., 2011 have found that the water and alcohol extractable matters were found to be 55 and 32% (w/w). The physicochemical parameters total ash, acid insoluble ash and water soluble ash value were found to be 4.75, 0.15 and 3.0% respectively. The loss on drying, pH in 1% solution and bitter value was found to be 2.15 5.73 and 3.53%.[2] Zahid et al., 2011 have demonstrated that the different extracts for phytochemical screening showed the presence of flavonoids, alkaloids, tannins and glycosides in methanol; flavonoids, alkaloids and glycosides in ether and alkaloids, and glycosides in chloroform extracts of *E. littorale.*[31]

Leela prakash and Mohan Dass, 2011 have identified that the qualitative phytochemical analysis of methanol extract of *E. axillare* showed the presence of various phytochemicals like alkaloids, glycosides, tannins, carbohydrates, proteins and amino acids, saponins and flavonoids. For TLC analysis different solvent systems were used to develop best separation of the phytoconstituents present in that extract. Maximum number of solvent systems gave good results except for Toluene: Ethyl acetate: Glacial acetic acid (12.5:7.5:0.5), Ethyl acetate: Butanol: Formic acid: Water (3:2:0.5:2), Ethyl acetate: Formic acid: Glacial acetic acid: H2O (100:11:11:26), Ethyl acetate: Ethanol: Acetic acid: H2O (8:1:1:8).[52]

Rama et al., 2012 found that the phytochemical analysis on extract was done by using different solvents and revealed the presence of steroids, terpenoids, alkaloids, phenolic compound, quinine, flavanoid, tannin and amino acid and identified by the basis of IR and gas chromatography-MS.The physicochemical parameters total ash, water soluble ash and acid insoluble ash value were found to be 6.20, 2.01 and 1.15% respectively[8]. Rana et al., have found in 2012 that the yields of the cold (room temperature) methanol and water extraction of the aerial parts of *E. littorale* were found to be 45.8% and 41.5% and that of hot methanol and water extraction were 44.0% and 43.6%. The amount of swertiamarin was determined in the four different crude extracts by using water: methanol (1:1) as the mobile phase in a flow gradient mode using RP-18 column to establish a better extraction method with a higher

yield of the compound of interest. Swertiamarin showed maximum absorption at λ_{max} 238 nm in three-dimensional ultraviolet absorption spectra using PDA detector. Cold water and methanol extracts were found to contain a higher amount (38.12±1.74% and 34.0±1.92%) of swertiamarin as compared to hot methanol and water extracts (30.76±1.41% and 20.13±0.84%).[53]

Ramesh and Dharaniyambigai, 2012 have identified that, the phytochemical analysis of the aqueous extract of *E. littorale* revealed the presence of alkaloids, flavonoids, saponins, carbohydrates, proteins, phenols, glycosides and tannins.[54] Sathishkumar et al., 2012 have reported that the methanolic extract of *E. littorale* showed the presence of flavonoids, polyphenols, phytosterol, alkaloids, terpenoids, tannins, saponins, carbohydrates, glycosides and protein. And presence of heavy metals such as arsenic, cadmium, lead and mercury were found below the WHO/FDA permissible limits.[55]

Mathur, 2013 has identified that the phytochemical screening showed the presence of various phytoconstituents alkaloids, glycosides, saponins, terpenoids, phenols, tannins, flavonoids, tritepenoids, steroids, and reducing sugar.[56] Saranya et al., 2013 found that the physicochemical parameters loss on drying, ash value, water soluble extractive and alcohol extractive values were found to be 0.198, 11.96, 27.65 and 24.57% (w/w) respectively in leaves of *E. littorale.*[5] Rathod and Dhale have found in 2013 that the phytochemical screening of the extracts and powder of *E. littorale* were found to contain protein, glycosides, alkaloids, tannins andphenolic compound, steroid reducing sugars, saponin and glycosides.[9]

Vinotha et al., 2013 have found that the ash values total ash; water soluble ash, acid insoluble ash and sulfated ash value were found to be 8.16 ± 0.1%, 2.75±0.1%, 1.89 ± 0.1% and 1.30 ± 0.1% respectively. The solubility percentage of *E. littorale* in aqueous hot extraction is higher (37.21±1.27%), when compared with ethanolic hot extraction (24.92±0.64%).[57] Further Vinotha et al., 2013 have identified that the preliminary phytochemical screening of hot and cold ethanol, methanol and aqueous extracts showed the presence of alkaloids, saponins, flavonoids, steroids, tannins, proteins, reducing sugar coumarins and quinones and absence of anthraquinones. Cold and hot water extracts showed the presence of fat and fixed oil. The total alkaloid and flavonoid contents were found to be 2.25 ± 0.01% and 25.34 ± 0.24% respectively and total saponin content was (Foaming Index) FI < 100.[58]

Analysis of organic solvent extracts of *E. littorale* revealed that the presence of total phenols, vitamin C and E and carbohydrates and the organic solvent extracts of *E. littorale* exhibited good antibacterial activities.[59] Selvaraj et al., have found in 2014 that the phytochemical analysis of leaf extract of *E. littorale* revealed the presence of steroids, quinones, cardiac glycosides, saponins, tannins, phenols, flavonoids, terpenoids and alkaloids and HPLC analysis in the leaf extract of *E. littorale* alsoproved the presence of the active principle namely swertiamarin.[60] Indumathi et al., 2014 have studied the *E. littorale* plant sample was extracted with 5 different solvent viz. ethanol, petroleum ether, chloroform, water and acetone extracts and found that the total amount of terpenoid present in the *E. littorale* sample was found to be 0.7% (70 mg/ g sample).[61]

Ahamad et al., 2014 have identified that the content of swertiamarin in hydro-alcoholic extract of *E. littorale* was found to be 12.62±2.18 % on dry weight basis of plant material and the developed HPLC-UV method showed a well-resolved peak of swertiamarin appeared at Rt 3.51±0.07 min with methanol-water (80:20) as mobile phase. The linear regression analysis data for the calibration curve showed good linearity in the concentration range of 100-1000 µg /ml with a correlation coefficient (r2) of 0.9994.[62]

Another review article mentioned that, *E. littorale* has a number of antioxidative phytochemicals as alkaloids, catechins, saponins, sterols, triterpenoids, phenolic acids, flavonoids and xanthones.[7]

Vigneswaran et al., 2017 mentioned in their review that *E. Littorale* possesses valuable bioactive compounds including alkaloids, saponins, catechins, sterols, phenolic acids, triterpenoids, flavonoids and xanthones. And also contains minerals like calcium, iron, potassium, phosphate, carbonate, chloride sulphate and silica.[63] *E. littorale* is rich source of alkaloids, catechins, saponins, sterols, triterpinoids, phenolic acids, flavonoids and xanthones. And it also contains minerals like iron, potassium, calcium, silica, phosphate, chloride sulphate and carbonate.[33]

Meshram et al., 2017 have estimated that 20.79% fiber content present in whole plant powder of *E. littorale* and whole plant extract contained 1.10% calcium, 0.12% phosphorus and 0.29% salts. Further, *E. littorale* contains gross energy value of 2474 kcal/kg.[64]

Selvam et al., 2018 have informed that the qualitative phytochemical analysis of *E. littorale* evidenced the presence of alkaloids, flavonoids, saponins, tannins, phytosterols, triterpenoids,

glycosides and phenolic compounds. In addition, the leaves extract is rich in minerals like magnesium, calcium, zinc, iron, sodium, and potassium and phosphorous.[65]

Toxicological Effects of *E. Littorale*

Text books stated that the *E. littorale* has very low toxicity and is a safe and effective anti spastic agent.[66,67]

Kulkarni et al., 1991 have reported that the graded doses (200, 500 and 2000 mg/kg bwt.) of swertiamarin were administered orally to various groups each containing 10 rats. On the first day, the animals were evaluated every 10 min for 4 hr. followed by 24, 48 and 72 hr. for any changes in spontaneous motor activity, gate, respiration, writhing, piloerection, etc., and up to 30 days for any mortality and no any side effects also reported.[68]

Khare, 2004 has mentioned that in a toxicity study, on the 3rd day after the oral administration of large doses of the *E. littorale* aqueous extract in alloxan induced diabetic rats and pigeons, liver and kidney showed early signs of degeneration. No toxicity has been reported with the standard dose in humans.[20] In 2004, Upadhyay and Goyal carried out a clinical trial with 84 diabetic patients who ingested 2g of *E. littorale* per day for 3 months; no adverse side effects were reported.[36]

Singh, 2008 has mentioned that the toxicity of gentiamine was determined and LD 50 for gentianine: LD50 (mice): 480mg/kg (oral); 300mg/ kg (abdominal injection); 250-300mg/kg (IV injection).[69] Previous in-vitro studies have found that the presence of heavy metals such as arsenic, cadmium, lead and mercury were below the WHO/ FDA permissible limits in whole plant of *E. littorale*. [2, 44], [50, 55]

Gupta et al., 2011 have found that the *E. littorle* extract possess significant antioxidant therapy to counteract mitochondrial and post-mitochondrial oxidative stress in the development of Gentamicin induced nephrotoxicity. That is suitable for chemoprevention of GM-induced renal damage.[70]

Nampalliwar and Godatwar, 2012 have found that in acute toxicity study of the aqueous extract of *E. littorale* was nontoxic up to recommended dose 5000mg/kg body weight orally as per OECD guidelines. The extracts did not show any signs of toxicity in streptozotocin induced diabetic albino rats.[71]

Acute toxicity study of the aqueous and chloroform extracts of *E. axillare* were nontoxic up to recommended dose 2000mg/kg body weight orally as per OECD guidelines no.423. The extract did not show any mortality or signs of toxicity in MES and PTZ induced seizures in albino rats.[72, 73] Dhanavathy and Jayakumar have authenticated in 2017 that oral administration of swertiamarin from *E. littorale* did not alter any parameters with special focus on histopathology which did not exhibit any lesions or abnormalities, which prove that no toxic adverse effects of the drug and further support the non-toxic nature of swertiamarin at the fixed dosage of 15, 25, 50 mg/kg in Wistar rats.[74]

Biological Activites of *E. Littorale*

Anti-diabetic activity

Vijayvargia et al., 2000 have found that the 30 days treatment with the aqueous extract of whole plant of *E. littorale* showed the significant (<0.001) reduction in plasma glucose level was accompanied with decrease in the level of glycosylated haemoglobin and glucose-6-phospatase activity in liver.[75]

Maroo et al., 2002 have found that asingle dose of aqueous extract of *E. littorale* (15 g dry plant equivalent extract per kg) had shown significant increase in the serum insulin levels in alloxan-induced diabetic rats at 8 hour further the results suggested the glucose lowering effect of aqueous extract of *E. littorale* to be associated with potentiation of glucose-induced insulin release through K (+)-ATP channel dependent pathway but did not require Ca(2+) influx.[76] Murali et al., 2002have suggested that aqueous extract of *E. littorale* (2 g/kg p.o.) is a potent herbal anti-diabetic and it produces an increase in insulin sensitivity, normalizes dyslipidaemia and provides nephron protection in neonatal non-insulin dependent diabetes mellitus (NIDDM) rats.[77]

Marooet al., 2003 have explained that the aqueous extract of *E. littorale* has a potent anti-diabetic agent without any toxic effect at particular dose (1.5 g dry plant equivalent extract/ 100 g body wt.) in alloxan induced diabetic rats.[78]

Upadhyay and Goyal, 2004 have found that pills prepared from *E. littorale* were administered to 84 patients with Type 2 Diabetes for three months. Estimation of various biochemical parameters showed that *E. littorale* reduced blood glucose as well as serum insulin levels and prevented the progression of complications in diabetic patients. Significant improvement in kidney function, lipid profile and blood pressure was observed suggesting that *E. littorale* is an effective herbal anti-diabetic.[36]

Srinivasa n et al., 2005 have found that there was a significant evidence for the anti-diabetic activity of oral administration of an aqueous *E. littorale* whole plant extract on some key carbohydrate metabolic enzymes and antioxidant defense in alloxan-induced diabetes in rats (150 mg kg (-1) body weight).[79]

Vishwakarma et al., 2010 have found in their study the dose dependent effect of 3 weeks treatment with hot and cold aqueous extract of *E. littorale* (0.5, 1 and 2 g/Kg) on streptozotocin induced type I diabetic rats (45 mg/ Kg, iv single dose) that there was a significant increase in fasting blood glucose levels and $AUC_{glucose}$ (area under the curves) associated with decrease in insulin levels and $AUC_{insulin}$ and a significant increase in serum cholesterol, and serum triglyceride. Further they concluded that *E. littorale* possesses potential anti-diabetic activity and improves lipid profile at a small dose of 0.5 g/Kg.[13]

Ratnasooriya et al., 2011 have identified that the fresh juice of whole plant of *E. littorale* showed there is no significant anti-glycation activity in vitro of 5 concentrations (25, 50, 75, 100, and 200 µg/ ml) of *E. littorale* in a bovine serum albumin / glucose system using fluorescence spectroscopy.[24]

Nampalliwar and Godatwar, 2012 have found that the aqueous and ethanolic extracts of *E. littorale* showed *s*ignificant anti-diabetic activity. In streptozotocin induced model, blood glucose levels of these extracts on 7th day of the study were 132.00±4.955 mg/dl and 163.3±28.69 mg/dl in comparison of chloroform extract (210.8±14.91 mg/ dl). In glucose loaded rats, aqueous extract exhibited glucose level of 176±3.724 mg/dl after 30 min. and 110±6.687 mg/ dl after 90 min. whereas the levels in ethanol extract treated animals were 166.66±3.403 mg/ dl after 30 min. and 148.83±4.615 mg/ dl after 90 min. These extracts also prevented body weight loss in diabetic rats. The drug has the potential to act as an anti-diabetic drug.[71]

Showkat R. Mir et al., 2016 have identified that swertiamarin was obtained from dried whole plant samples of *E. littorale* and it was effective in the achieving stricter glycemic control in carbohydrate challenged mice through the inhibition of carbohydrate metabolizing enzymes.[80]

Hypolipidaemic Activity

Gopal et al., 2004 have found that the aerial part of the *E. littorale* powder reduced the hypolipidaemia at significant level and also reduced the lipid peroxidation and HDL-cholestrol level in serum in p-dimethyloaminoazobenzene induced hepatoma rats (1 mg/Kg body weight).[81] The hypolipidaemic and antioxidant effect of *E. littorale* aqueous extract (1.5 g/100g body weight/day, p.o.) in cholesterol fed rats is being reported for the first time by Vihas et al., 2005.[82]

Vasu et al., 2005 studied that the aqueous extract (1.5 g/100g body weight/day, p.o) of *E. littorale* was administered to rats along with hypercholesterolaemic diet for 6 weeks for the hypolipidaemic and antioxidant effect and they have found that the treatment with the extract showed a significantly decreased in activities of erythrocyte catalase, superoxide dismutase and lipid peroxidation levels, with an increase in reduced glutathione levels as compared to cholesterol fed untreated rats. Liver and kidney cholesterol levels and triglyceride levels were also decreased in *E. littorale* treated rats.[83]

Vaidya et al., 2009 have suggested that swertiamarin (50 and 75mg/kg) which was isolated from *E. littorale* possess high antiatherogenic potential and effective cholesterol lowering agent and inhibition of HMG-Co A reductase may be one of the main mechanisms of hypolipidemic effect of swertiamarin in the high cholesterol feed rats.[84]

Thirumalai et al., 2011 have found that the aqueous leaf extract of *E. littorale* at a dosage of 250 mg/kg body weight showed that the levels of cholesterol, triglycerides and free fatty acids were decreased in serum and liver tissue, levels of TBARS and lipid hydroperoxide were decreased, and liver antioxidant enzymes were increased in liver tissue and suggested *E. littorale* has potent restorative effect on hyperlipidaemic and oxidative stress against ethanol induced hepatic injury in albino rats.[85]

Hepatoprotective Activity

Vishwakarma and Goyalm, 2004 have confirmed that the treatment with aqueous extract of *E. littorale* enhances the recovery from CCl4 -induced hepatotoxicity and maintaining normal function of the liver in Swiss albino mice.[86]

Senthil kumar et al., 2005 have found in their study of anti-hepatotoxic activity that the alcohol extract of the whole plant of *E. littorale* showed a remarkable hepatoprotective effect against CCl_4-induced hepatic damage in rats which activity was evaluated by using biochemical parameters, such as serum glutamate pyruvate transaminase, serum glutamate oxaloacetate transaminase, alkaline phosphatase, total bilirubin, and γ.-glutamate transpeptidase.[87]

Gopal and Udayakumar, 2008 have found that the aerial part of the *E. littorale* showed the hepatoprotective effect on p-dimethyloaminoa-zobenzene induced hepatocarcinoma rats.[88]

Barani srinivasan et al., 2009 have found that the leaves of *E. littorale* and *Eclipta alba* combine (1:1) at dose level of 250 mg^{-1} body weight produced significant hepato-protection and anti-oxidative effect on ethanol induced oxidative stressin wistar male albino rats.[89] Gite et al., 2009 have found that the water extract of aerial parts of *E. axillare* shown very significant hepatoprotection against CCl4-induced hepatotoxicity in albino rats in reducing

serumtotal bilirubin, SALP, SGPT, SGOT levels and liver homogenates LPO, SOD, CAT, GPX, GST and GSH levels.[90]

Jaishree et al., 2010 have found that the ethyl acetate extract of *E. axillare* (100 / 200 mg/Kg body weight) has shown the more potent hepatoprotective activity against CCl4 induced hepatic injury in rats.[91] Jaishree and Badami, 2010 have observed that swertiamarin isolated from *E. axillare* possesses significant hepato-protective properties against D-Galactosamine induced hepatotoxicity in rats given at 100 and 200mg/kg body weight orally for 8 days.[92] Gite et al., 2010 have demonstrated that the methanol and water extracts of aerial parts of *E. axillare* have shown very significant hepatoprotection against CCl4-induced hepato-toxicity in albino rats in reducing serum total bilirubin, direct bilirubin, SGPT and SGOT levels.[93] Gite et al., 2010 have found that the water extract of aerial parts of *E. axillare* have shown very significant hepatoprotection against paracetamol-induced hepatotoxicity in albino rats in reducing serum total bilirubin, SALP, SGPT, SGOT levels and liver homogenates LPO, SOD, CAT, GPX, GST and GSH levels.[94]

Srinivasan and Sreenivasan, 2011 have found that the aqueous extract of the leaves of *E. littorale* showed the significant hepato-protective activity and antioxidant effect on ethanol induced oxidative stress in male albino rats (7.9g/Kg body weight).[95]

Anti-inflammatory activity

Sadique *et al*., have confirmed in their studies which were donein 1987 and 2000 that the *E. littorale* showed 54% anti-inflammatory activity for a dose of 100mg/ 100g body wt. in carrageenan induced acute inflammation in rats; in chronic inflammation of cotton pellet granuloma exerted 30% anti-inflammatory activity at the above dose.[96, 97]

Arivukkarasu *et al*., 2009 have proved that the alcohol extract at a concentration of 300 and 600 mg kg-1 p.o., and its ethyl acetate fractions at 25 and 50 mg kg-1 p.o. showed a significant dose dependent anti-inflammatory activity in carrageen induced rat hind paw edema as well as formalin induced rat hind paw oedema chronic model in rats. This study showed that the alcohol extract of *E.littorale*, and its ethyl acetate fractions, exhibited significant anti-inflammatory activity.[98] Shivakumar et al., 2009 have also confirmed that the petroleum ether and methanol extracts of *E. littorale* exhibited significant anti-inflammatory activity against 1% yeast suspension induced inflammation in rat paw after 24 hours.[99]

Roy *et al*., 2010 have found that the methanolic extract of the aerial parts of *E. littorale* (200 mg/kg and 400 mg/kg po.) possessed antiulcer activity, and the anti-inflammatory activity against aspirin, ethanol, and pyloric ligation-induced ulcers in rats and bovine serum albumin denaturation.[100]

Leelaprakash and Dass, 2011 have mentioned that the methanol extract of whole plant of *E. axillare* showed the potential source of anti-inflammatory agents and in-vitro anti-inflammatory activity which was evaluated using albumin denaturation assay, proteinase inhibitory activity, membrane stabilization, and anti-lipoxygenase activity at different concentrations range of 100-500µg/ml.[52]

Kanthasri et al., have confirmed in 2014 that the ethyl acetate active fraction (200 mg/ Kg p.o) of *E. littorale* leaves showed significant analgesic action (<0.01) and reduction of pain in comparison with control group and also significantly (P<0.05) anti-inflammatory activity on carrageenan induced paw oedema models in wistar rats.[101]

Analgesic and Anti-Arthritic Effect

Shabi et al., 2014 have proved that the analgesic activity in hot plate and tail immersion method revealed that the 85% methanolic extract of the whole plant of *E. littorale* exhibits significant activity at 150 mg/kg body weight and the effect is found to increase dose dependently. In Freund's adjuvant induced arthritis, *E. littorale* is found to decrease the paw volume (15.81%). Significant protection is also observed by elevating antioxidant enzymes. Further, they concluded that, the 85% methanolic extract of *E. littorale* possesses significant analgesic and anti-inflammatory activities in Freund's adjuvant induced arthritic model in rats.[102]

Antimicrobial Activity

Deore et al., 2008 have observed that chloroform, ethyl acetate and hydro alcoholic extracts of *E. littorale* showing prominent anti-microbial activity against all the selected microorganism as *Staphylococcus aureus*, *Bacillus subtilis, Proteus vulgaris, Escherichia coli, Pseudomonas aeroginosa, Shigella sonnei, Aspergillus niger and Candida albicans*.[23]

Anita et al., 2010 have confirmed that the methanolic extract of *E. axillare* leaves exhibited antibacterial effect against all of the bacteria and also shows good antifungal activity against *Candida albicans* and *Aspergillus niger*.[103] Rita et al., 2010 have stated that the aqueous and ethanol extracts of leaves, whole plant and secondary metabolites of *E.littorale* showed better antimicrobial activity against three each test bacterial and three fungal species.[104]

Gopal et al., 2011 have identified in their study of evaluation for in vitro antifungal activity of different extracts of the whole plant of *E. littorale* that

the ethanol extract showed pronounced activity against *Aspergillus niger* and *Candida albicans* than other extracts as hexane, chloroform, ethylacetate, ethanol and aqueous extract of the whole plant of *E. littorale*.[105] Praveena and Sudarasanam, 2011 have observed that ethyl acetate and methanol extracts of *E. littorale* showed prominent in-vitro antimicrobial activity against selected microorganisms such as four Bacterial species (*Staph aureus*, *Pseudomonas aeroginosa, Salmonella typhi* & *Shigella sonnei*) and two Fungal strains (*Aeromonas hydrophila & Candida albicans*).[106]

Pitchamuthu et al., 2012 have reported that the chloroform extracts different parts of *E. littorale* showed the highest antibacterial activity. Among leaf, stem and root extracts, the stem extracts showed maximum antibacterial activity. All of the used extracts had no significant antifungal activity against *Aspergillus fumigates* and *Aspergillus flavus*. They concluded that the findings of the study indicate *E. littorale* could also be a new source for antibiotics discovery.[107] Thayalini et al., 2012 have mentioned that the aqueous extract of *E. littorale* showed growth inhibitory action against Methicillin resistant *Staphylococcus aureus*.[108]Leelaprakash and Mohan Dass, 2012 have found that the methanol extract of *E. axillare* showed good antibacterial and antifungal activity on Gram positive, Gram negative and some fungal strains have been performed by Disc diffusion method and it may be attributed due to the presence of phytochemicals it may be used as antimicrobial agents.[52]

Mathur, 2013 has identified that the ethanol extract of the whole plant of *E. hyssopifolium* showed the highest zone of inhibition against Human pathogenic microorganisms among all the petroleum ether, chloroform, *n*-Butanol, ethanol and aqueous extracts. With *Escherichia coli,* zone of inhibition was 20.0mm, with Coagulase (+) *Staphylococci* it was 27.3 mm., with Coagulase (-) *Staphylococci* 26.6 mm., with Pseudomonas aeruginosa 25.0 mm., with Enterococcus sp. 23.6 mm., with *Candida albicans* and *Candida parapsilosis* it was 22.0 mm and 20.5 mm respectively.[56]

Indumathi et al., 2014 have reported in their study of the antimicrobial activity of the terpenoid extract of *E. littorale* has shown that the considerable diameter of zone of inhibition was observed against *E. coli and B. Subtilis*.[61] Shanmugapriya and Priya, 2014 have reported that the antibacterial activity exhibited by chloroform, methanol and aqueous leaves extracts of *E. axillare*against *S. aureus*, *E. coli*, *Pseudomonas aeruginosa*, *P.vulgaris* and *K. pnemoniae*.[109]

Lavanya and Deepa 2015 have proved that *E. littorale* flower extract showed maximum zone of inhibition against all the selected bacterial strains as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus cereus* and *Bacillus subtilis*.[110] Patel et al., 2015 have reported that the stem and root, of ethyl acetate extract of *E. littorale* showed the significant antimicrobial activity against pathogenic microorganism by disk diffusion method. The highest antimicrobial activity of root extract show against *salmonella typhi* (20 mm) and stem extract against *staphylococcus aureus* (12 mm) due to the various phytochemicals present in extract.[111]

Mullai and Karthikeyan, 2017 have suggested that the biologically active molecules phytol from the methanolic leaf extract of *Enicostemma axillare*, acts against the multi-drug resistant bacterial strains (antibacterial activity) such as E. coli and *Klebsiella pneumoniae*.[112]

Kowsalya et al., 2019 have found that Ag NPs and Zinc synthesized using an aqueous extract of *Enicostemma littorale* have potential antibacterial activity against both Gram Negative and Gram Positive bacteria.[113]

Anthelmintic activity

Vidyadhar et al., 2010 have found in their study of evaluation for anthelmintic activity of different extracts of the whole plant of *E. littorale* that the ethanol extract showed significant pronounced activity followed by ethyl acetate>water >chloroform >hexane extracts at different concentrations like 25, 50, 100, and 200mg/ml.[16]

Mishra et al., 2011 have examined that the ethanolic extract of aerial parts of *E. littorale* {Five concentrations (2.5, 5, 10, 25 & 50 mg/ml)} was more potent anthelmintic activity than the petroleum ether extract on adult Indian earthworms, *Pheretima posthuma*, using albendazole as reference standards.[114]

Antioxidant Activity

Prince and Srinivsan, 2005 have reportd in their study investigates the effect of oral administration of an aqueous *E. littorale* whole plant extract on antioxidant defense in alloxan-induced diabetes in rats that the oral administration of aqueous *E. littorale* whole plant extract (1 and 2 g/kg) to diabetic rats daily for 45 days significantly decreased blood glucose, TBARS, HP and increased GSH, SOD, catalase and GPx. *E. littorale* extract at the dose of 2 g/kg was more effective than 1 g/kg. Insulin (6 units /kg) administration to diabetic rats for 45 days brought back all the parameters to near normal status and they concluded that the *E. littorale* had antioxidant potential.[41]

Jaishree et al., 2008 have found that the successive petroleum ether, chloroform, and ethyle acetate extracts of *E. axillare* exhibited potent in vitro antioxidant activity in ABTS, H_2O_2, nitric oxide and hydroxyl radical using the deoxyribose and lipid peroxidation methods.[115]

Sathiskumar et al., 2009 have found that the different drying treatment especially microwave, treated plant material led to significant reduction ($P<0.05$) in antioxidant properties in methanolic extract of *E. littorale* as compared to that of hot water extract, which appeared to exhibit significantly stronger antioxidant potential ($P<0.05$) even in dried plant materials due to greater solubility of compounds, breakdown of cellular constituents as well as hydrolysis of tannins.[34] Jaishree and Badami, 2009 have observed that swertiamarin which was isolated from the ethyl acetate extract of *E.axillare* possess good in-vitro antioxidant activity in ABTS and hydrogen peroxide methods when compare with the seven different methods.[116]

Jaishreeet al. (2010) have found that the ethyl acetate extract of *E. axillare* has shown potent in vitro antioxidant activity and found to contain 7.26% of a bitter secoiridoid glycoside, swetiamarin.[91] Jaishree and Badami, 2010 have identified that swertiamarin isolated from *E. axillare* possesses significant antioxidant activity against D-Galactosamineinduced liver injuryin rats.[92]

Researchers have stated in 2011 that the flowers of *E. littorale* have strong antioxidant potential when compare with different parts of that plant.[117] Further, Akhtar, 2011 has also summarized about antioxidant potential of dried *E. littorale* in Pakistan Journal of Biological Sciences.[118]

Ramesh and Dharaniyambigai, 2012 have found that, the in-vitro antioxidant activities as DPPH, ABTS & FRAP assay results indicated the antioxidant potential of aqueous extract of *E. littorale*.[54] Krishnaveni and Mohandass, 2012 reported in their study that the ethanolic, methanolic and petroleum ether extracts of *E. axillare* exhibited potent in vitro antioxidant activity and have shown higher values in total phenol and flavanol content.[119]

Selvaraj et al., 2014 have observed that the total phenol and terpenoid content in leaf extract of *E. littorale* were found to be 16.32 mg Gallic acid equivalents/g and 71.0 mg/g respectively and the acetone leaf extract also showed significant radical scavenging activity (DPPH) among five different solvent extracts when compared with that of synthetic antioxidant BHT as a positive control.[60]

Amit Vaibhav et al., 2017 have stated that their pilot study result showed that standardized aqueous extract of *E. littorale* exhibit excellent potential to minimize the oxidative stress when administered orally in Metabolic Syndrome patients.[120]

Vinotha et al., 2018 have authenticated that, hot methanol and aqueous extracts of *E. littorale* showed low in vitro antioxidant activity in DPPH, ABTS and FRAP methods in comparison to the standard trolox.[121] Selvam et al., 2018 have evidence in their study that the ethanolic extract of *E.littorale* possess significant antioxidant properties and the leaves may be considered as an important source for the screening of natural lead molecules.[65]

Diabetic neuropathy activity

Bhatt et al., 2009 have found in their study of the protective effects of *E.littorale* (2.5g kg-l), a hypoglycemic and antioxidant herbal medicine in alloxan-induced diabetic neuropathy in male Charles foster rats that nociceptive responses were compared by formalin and tail flick in hot immersion test in both diabetic and non-diabetic rats. Treating with *E.littorale* extract for 45 days significantly improved with nociception in diabetic rats. The changes in lipid peroxidation and antioxidant enzymes like SOD, GPx and CAT levels, decrease in Na-K+ ATPase activity were also restored by *E. littorale* treatment. This study provides an experimental evidence for the preventive effect of *E. littorale* on nerve function and oxidative stress in animal model of diabetic neuropathy.[122]

Diabetic nephropathy activity

Sonawane et al., 2010 have confirmed that the treatment with aqueous extract of *E.littorale* (1 g/kg, p.o.) and swertiamarin (50 mg/kg, p.o.) daily for 3 weeks significantly decreased serum urea and creatinine and other parameters associated with the development of diabetic nephropathy in type 1 diabetic rat. They have also found considerable improvement in histology of glomerular function of aqueous extract of *E. littorale* and swertiamarin-treated animals.[123]

Anti-hyperinsulinemic activity

Gohil et al., 2008 have found that the aqueous extracts of *Aegle marmelos* and *E. littorale* reduce hyperglycaemic conditions in diabetic animal. Insulin resistance was induced in wistar rats by fructose rich diet (60% for 15days). Treated groups received fructose diet plus aqueous extracts *A. marmelos* (500 mg/kg/day) and *E. littorale* (2 g/kg/day). Body weight, serum glucose, insulin, C-reactive protein and triglycerides levels were estimated after treating with an extract and they reported that the fructose feeding for 15 days significantly increased the serum glucose, insulin, C-reactive protein and triglycerides levels compared to control. Administration of aqueous extracts of *A. marmelos* and *E. littorale* for 15

days prevented hyperglycemia and hyperinsulinemia induced by a diet high in fructose.[124]

Anti-tumour activity

Kavimani and Manisenthilkumar, 2000 have stated that the methanolic extract of *E. littorale* indirectly inhibited tumour cell growth and it was examined on the peritoneal exudates cells of the normal mice. Methanolic extract of *E. littorale* found to enhance potential cell counts. These results demonstrated the indirect effect on the cells, probably mediated through enhancement and activation of macrophages or through some cytokine product inside the peritoneal cavity produced bymethanolic extract of *E. littorale* treatment.[125]

Immunomodulatory

Saravanana et al., 2012 have found that the animals treated with methanol extract of *E.axillare* showed a significant (P≤0.05) increase in weight of the thymus and spleen. The total leukocyte and lymphocyte count was increased significantly (P<0.005) by the treatment. There was no significant alteration in neutrophil count and the findings suggested that the methanol extract of *E. axillare* acted on both humoral and cell mediated immune functions and decreased the release of pro-inflammatory cytokines in the peritoneal macrophages.[126]

***E. littorale* as a new target for islet neogenesis**

Gupta et al. 2010 have demonstrated an islet neogenic property of one herbal plant *E.littorale*. An active herbal compound SGL-1 was isolated and purified from extract of *E.littorale* and used to differentiate two model stem cell lines PANC-1 and NIH3T3 which showed tremendous islet neogenic potential and significant islet yield compared to control serum free medium. Morphological, molecular and immunological characterization of newly generated islet like cellular aggregates proved them differentiated and positive for islet hormones. Functional characterization of ICA's confirmed significant glucose responsive insulin release. They concluded that this preliminary data does offer exciting possibility of alternate source for increasing islet mass which can be used for the treatment of diabetic patients. [127]

Antinociceptive activity

Jaishree et al., 2009 have demonstrated in their study of in vivo anti-nociceptive activity of swertiamarin isolated from *E. axillare* that using three different methods in mice. In the hot plate method, a significant increase in the latency period was observed for the treatment with swertiamarin at 100 and 200 mg/kg after 30 and 45 min. The percent protection observed after 45min was 109.42, 147.42 and 157.14, respectively, for the standard paracetamol and swertiamarin at 100 and 200 mg/kg body wt. treatments. A significant increase in the tail withdrawal reflex was observed for the swertiamarin treatment at both the doses with percent protections of 150 and 200, respectively. In both these methods, swertiamarin produced potent activity than that of standard paracetamol.[128]

Antidepressant activity

Doss and Dharaniyambigai, 2016 has found in their study that sodium orthovanadate induces depression in animals and also establishes the antidepressant activity of *E. littorale*.[129]

Antiepileptic activity

Shalini and Saravana Kumar, 2011 have suggested that the chloroform extract of whole plant of *E. axillare* significantly increased the monoamines on rat brain, which may be decreased the susceptibility to Maximal Electroshock and Pentylenetetrazole induced seizure models in albino wistar rats.[130] Shalini et al., 2011 have reported that the antioxidant properties of chloroform extract of *E.axillare* (200 & 400mg/kg) delays the generation of free radical in MES & PTZ induced epilepsy in Albino wistar rats (150-200g).[131]

Anti HIV activity

Praveena et al., 2014 have identified in their study of anti-HIV activity of the whole plant of *E. littorale* that the methanolic extract of *E. littorale* showed prominent anti-HIV activity was determined using in-vitro studies such as TZM-bL assay and PM1 assay against on HIV-1 induced cytopathic effects in cell culture.[132]

Anti-Dermatophytic activity

Jeyam et al. 2013 have demonstrated in their in vitro study of evaluate the anti-dermatophytic activity of *E. littorale* that significant results were observed with the petroleum ether extract of the aerial parts of the *E. littorale* at a concentration of 3000 µg/ ml against *Microsporum gypseum*.[133]

Anti-Hypertensive activity

Anwar et al., 1996 have found that the methanol extract of the *E. littorale* has shown no significant improvements on the blood pressure of rats and ileum of Guinea-pig.[48] Shanmukha et al., 2017 have suggestedthat the 70% ethanolic extract of *E.littorale* imparted a protective action against adrenaline induced hypertension in rats and it has profound hypotensive activity.[134]

Antiplasmodial activity

Soni and Gupta, 2009 have reported that their study of antiplasmodial activity of methanolic extract of *E. littorale* represented the potential anti-malarial action of plant against *Plasmodium falciparum* and its active phytoconstituent, may give new lead to

researchers in field of anti-malarial drug discovery.[135]

Jude E. Okokon et al., 2012 have demonstrated that, the crude extract (260-780 mg/kg) and fractions (chloroform and aqueous; 520 mg/kg) of *E. littorale* possesses considerable antiplasmodial activity against chloroquine-sensitive *Plasmodium berghei* infections in mice and antipyretic activity against dinitrophenol, amphetamine and yeast-induced pyrexia.[136]

Anti-Obesity activity

Garg and Singh, 2014 have observed reduction in body weight gain, feed intake, BMI, obesity index, serum lipids; glucose and decrease body fat pad weigh suggested that the aqueous and ethanol extracts of *E. littorale* exhibited significant anti-lipase and anti-obesity activity in high fat diet induced obesity in rats.[137]

Antifertility activity

Ramaiyan Dhanapal et al., 2012 have stated that the ethanolic (70% v/v) leaves extracts of *E. axillare* (375 and 750 mg/kg) reversibly inhibited spermatogenesis and steroid genesis indicating reversible antifertility activity in adult male Wistar albino rats [138].

Antiedmatogenic activity

Jaishree and Badami, 2009 have confirmed that swertiamarin which was isolated from the ethyl acetate extract of *E.axillare* possess antiedmatogenic activity in carrageenan, formalin, and histamine induced paw oedema in rats.[116]

Other related studies

Vishwakarma et al., 2004 have mentioned that *E. littorale* whole plant was found to be a rich source of swertiamarin (7.7% w/w) and their developed simple HPTLC method is suitable for quantification of swertiamarin in samples containing amounts ranging from 0.15 to 7.7% (w/w).[139]

Laxman et al., 2010 have mentioned that their pharmacognostic evaluation study could be useful in setting some diagnostic indices for identification and preparation of the monograph of the *E. littorale.*[140]

Alam et al., 2019 have confirmed that the proposed validated HPLC method according to the ICH guidelines is suitable for the quantification of swertiammarin in both methanolic extract of *E. littorale* and marketed formulations.[141]

DISCUSSION

The World Health Organization (WHO) encourages, recommends and promotes the use of traditional herbal remedies in National health care programmes because these medicines are easily available, inexpensive, and faith of people in their therapeutic properties.[142] However, plants used in the preparation of herbal remedies are very complex and vary in their composition and phytochemical content. The therapeutic activity of any herbal remedy will depend on (a) a proper identification of the plants used in its preparation, (b) chemical constituents that can vary according to age, geographical location, season, harvesting process, etc., (c) any adulterants in the preparation.[6] Therefore, it is very important to have an understanding of all parameters that would help to develop standardized preparations of *E. littorale* that is to be used for therapeutic purposes.

The secondary metabolites such as alkaloids, flavonoids, lignins, terpenoids, steroids, glycosides, coumarins and phenols in plant materials produce the curative effect when they are used in Traditional medical practice.[143]Secondary metabolites were found in good proportion in alcoholic and aqueous extracts when compared. These secondary metabolites may be responsible for various pharmacological effects of different extracts of preparations. Such phytochemical screening was helpful in prediction of nature of drugs.[144]The vast and versatile pharmacological effects of medicinal plants are basically dependent on their phytochemical constituents. According to the numerous studies, *E.littorale* has multi different therapeutic pharmacological actions.

Evaluation of physicochemical parameters of drugs is essential for detection of adulteration or improper handling of drugs as stated in African Pharmacopoeia.[46]

Fluorescence is an important phenomenon exhibited by various chemical constituents present in plant material. Some constituents show fluorescence in the visible range in many natural products (e.g., alkaloids like berberine), which do not visibly fluoresce in day light. If the substances themselves are not fluorescent, they may often be converted into fluorescent derivatives by applying different reagents; hence some crude drugs are often assessed qualitatively in this way and it is an important parameter of pharmacognostical evaluation.[145- 147]

Numerous previous phytochemical screening studies have shown that compounds such as triterpenoids, flavonoids, alkaloids, saponins, protein, polyphenols,carbohydrates and coumarins found in aqueous extract[13,50] and methanol extracts of *E. littorale*.[46, 49, 55, 94]

Contamination by toxic metals can either be accidental or intentional. Lead, cadmium, mercury, thallium and arsenic have been shown to be contaminants of some herbal ingredients. Their presence can be attributed to many causes, including environmental pollution, and can pose clinically relevant dangers for the health of the user and should

therefore be limited [6], [148,149]. Therefore, limit tests for such toxic metals are essential for herbal ingredients.[150] The therapeutic value of any drug depends not only on its clinical efficacy, but also on its lack of side effects.[147] Hence, heavy metals need to be evaluated in such preparations. Researchers stated that the *E. littorale* has very low toxicity and is a safe and effective to use as medicinal ingredient.

According to these information's, the systematic review was carried out for the monographic documentation of the multi therapeutic uses and pharmacognostic research work about the plant *Vellarugu* (*E. littorale*).

CONCLUSION

Based on these numerous studies related review provides the *E. littorale* has the number of anti-oxidative phytochemicals, physiochemical properties,chemical constitutions, very low toxicity and is a safe, presence of heavy metals were below the WHO/ FDA permissible limits, and therapeutic pharmacological actions such as anti-diabetic, antioxidant,hypolipidaemic, hepatoprotective, anti-microbial, anti-inflammatory, immunomodulatory, analgesic, anti-arthritic, anti-tumourand etc. This monograph may provide and confirmed the documentary evidence for multiple medicinal & therapeutic uses and pharmacological effects of the *Vellarugu* (*E. littorale*). Longitudinal scientific studies should be carried out in human to prove its clinical standards in the management of the multiple diseases in future.

ACKNOWLEDGEMENT

Author would like to specifically acknowledge and sincere gratitude Dr. (Mrs.) Sri Ranjani Sivapalan, Retired Senior Lecturer, University of Jaffna for inspiration, encouragement and constructive criticism-introducing to the area of medicinal plants via a never ending enthusiastic help, high-impact guidance to this publication.

REFERENCES

1) Refaz Ahmad Dar, Mohd Shahnawaz, Parvaiz Hassan Qazi. General overview of medicinal plants: A review. The Journal of Phytopharmacology. 2017; 6(6): 349-351.
2) Pandya K, Maniar K, Soni H, Bhatt S, Patel P, Solanki B, Gurav N. Standardization of Anti-diabetic Ayurvedic herbo-mineral formulation. International Journal of Pharmaceutical Sciences Review and Research. 2011;10(1):174-186.
3) Fazal H, Ahmad N, Ajab Khan M. Physico-chemical, Phytochemical Evaluation and DPPH- Scavenging Antioxidant potential in Medicinal Plants used for herbal formulation in Pakistan. Pak. J. Bot.2011; Special Issue, 43:63-67.
4) Ahmed E, Arshad M, Ahmed M, Saeed M, Ishaque M. Ethnopharmacological survey of some medicinally Important plants of Galliyat areas of NWFP. Pakistan Asian Journal of Plant Sciences. 2004; 3: 410-415.
5) Saranya R, Thirumalai T, Hemalatha M, Balaji R, David E.Phrmacognosy of *Enicostemma littorale:* A review. Asian Pacific Journal of Tropical Biomedicine.2013; 3(1): 79-84.
6) W.H.O. Research Guidelines for Evaluating the safety and Efficacy of Herbal Medicines. World Health Organization, Manila. 1992.
7) Amarnath Shukla.A Review of a potential hypoglycemic plant *(Enicostemma littorale Blume*). European Journal of Biomedical and Pharmaceutical Sciences.2015;2(1):154-165.
8) Rama V, Clarina T, Maheswari M, Nalini Mabel GD. Pharmocognosy and Phytochemical study of *Enicostemma Littorale Blume*. American Journal of Pharm Tech Research. 2012; 2(5): 599-604.
9) Rathod MC, Dhale DA.Pharmacognostic characterization of *Enicostemma littorale Blume*. Int. J. Res. Ayurveda Pharm. 2013; 4 (6): 893-896.
10) Murukesu Mudaliyar KS.Materia Medica I (Vegetable kingdom). *Siddha maruthuva varrium,* Chennai 600106; 4th ed.1988.p.607.
11) Murukesa Mudaliyar KS.*Agasthyar Gunavagadam*. Department of Indian Medicine and Homeopathy, Government of Tamil Nadu; 7th ed. 2003.p.844.
12) Kannusamipillai S. *Siddha Vaidthiya Patharththa Guna Vilakam*, (*Moolavarkkam*). B. Rathinanajakar & Sons, Chennai; 6th ed.1998. p.671.
13) Vishwakarma SL, Sonawane Rakesh D, Rajani M, Goyal RK. Evaluation of effect of aqueous extract of *Enicostemma littorale* blume in streptocin-induced type I diabetic rats. Indian Journal of Experimental Biology.2010; 48:26-30.
14) Nadharni K. Indian Materia Medica. Vegetable kingdom. Vol. I. Bombay Popular Prakashan; 2002. p. 485, 1292-1294.
15) Kirtikar KR, Basu BD. Indian Medicinal Plants. Vol. III (2). Bishen Singh Mahendra Pal Singh, Delhi; 2003.p. 1655-1656, 1774-1777.
16) Vidyadhar S, Saidulu M, Gopal TK, Chamundeeswari D, Umamaheswararao David Banji. In Vitro Anthelmintic activity of the whole plant of *Enicostemma littorale* by using various extracts. International Journal of Applied Biology and Pharmaceutical Technology. 2010;1(3): 1119-1125.
17) Patel TP, Soni S, Parikh P, Gosai J, Chruvattil R, Gupta S.*Swertiamarin:* An Active Lead from *Enicostemma littorale* Regulates Hepatic and Adipose Tissue Gene Expression by Targeting PPAR-γ and Improves Insulin Sensitivity in

Experimental NIDDM Rat Model. Evidence-Based Complementary and Alternative Medicine. 2013;1:1-11.

18) Abirami P, Gomathinayagam M.A Review on *Enicostemma littorale.* Pharmacology online. 2011; 1: 75-83.

19) Dymock William, Warden CJH, Hooper David. Pharmacographia Indica. Calcutta; Thacker, Spink & Co. 1893. 2:p. 1-546.

20) Khare CP. Indin Herbal Remedies, Rational Western Therapy, Ayurvedic and Other Traditional Usage, Botany. Springer-Verlag Berlin Heidelberg New York; 2004.p.203-204, 480-481.

21) Gupta AK, Tandon N, Sharma M. Quality Standards of Indian Medicinal Plants. Indian Council of Medical Research, New Delhi; 2005. 3:p.203-211.

22) Gentian Research Network, USA.Gentian Research Network and Rutgers University. 2002-2008. http://gentian.rutgers.edu/genera

23) Deore SL, Khadabadi SS, Bhagure L, Ghorpade DS. In vitro antimicrobial and antioxidant studies on *Enicostemma axillare (Lam.)* Raynal. Leaves. Natural Product Radiance. 2008;7(5): 409-412.

24) Ratnasooriya WD, Somarathna K, Premakumara G, Ediriweera E. Lack of antiglycation activity of fresh juice of whole plant of *Enicostemma axillare (Lam.)* Raynal. Journal of Pharmaceutical Negative Results. 2011; 2(2): 55-57.

25) Dassanayake MD, Fosberg FR. A Revised Handbook to the Flora of Ceylon. New Delhi, Oxford and IBH Publishing Co.1981.

26) Lakshmi PTV, Annamalai A, Ramya C.A study on the Genetic Diversity Analysis of a medicinally potential herb-*Enicostemma littorale* Blume (Gentianaceae). International Journal of Pharma and Bio Sciences. 2011; 2(4): 238-445.

27) Shukla A. Review of a potential hypoglycemic plant *(Enicostemma littorale Blume).* European Journal of Biomedical and Pharmaceutical Sciences.2014;2 (1): 154-165.

28) Padmanabhan DD, Regupathy, Veni SP. Gynoecial ontogeny in *Enicostemma littorale* Blume. Proc. Indian Acad. Sci. 1978; 87: 83-92.

29) Sankaranarayanan S, Bama P, Ramachandran J, Kalaichelvan PT, Deccaraman M, Vijayalakshimi M, Dhamotharan R, Dananjeyan B, Sathya Bama S.Ethno botanical study of Medicinal plants used by traditional users in Villupuram district of Tamil Nadu. India Journal of Medicinal Plants Research.2010; 4 (12): 1089-1101.

30) Gupta RS, Singh D. Hepatomodulatory role of *Enicostemma littorale Blume* against oxidative stress induced liver injury in rats. African Journal of Agricultural Research. 2007;2:131-138.

31) Zahid Z, Sagar DD, Aniruddha PP, Subar K, Ahmed RZ. Phytochemical screening of plant of *Enicostemma axillare.* International Journal Research and Pharmacy. 2011; 2(1):175-176.

32) Jeeva S, Kiruba S, Mishra BP, Venukopal N, Dhas SSM, Regini GS, Kingston C, Kavitha A, Sukumaran S, Raj ADS,Laloo RC. Weeds of Kanyakumari district and their value in rural life. Indian Journal of Traditional Knowledge. 2006; 5(4): 501-509.

33) Mishra N, Kaushal K, Mishra RC, Sharma AK.An Ayurvedic herb: *Enicostemma littorale Blume* - A review article. Journal of Medicinal Plants Studies. 2017; 5(1):78-82.

34) Sathishkumar R, Lakshmi PTV, Annamalai A.Effect of drying treatment on the content of antioxidants in *Enicostemma littorale* Blume. Research Journal of Medicinal plant. 2009; 3:93-101.

35) Dalit Database. Community Food System Data Table #200. Quebec, Canada: McGill University Centre for Indigenous Nutrition and Environment (CINE) 2006.

36) Upadhyay UM, Goyal RK. Efficacy of *Enicostemma littorale* in type 2 diabetic patients. Phytotherapy Research. 2004; 18: 233-235.

37) Petel SS, Shah RS, Goyal RK. Antihyperglycemic, antihyperlipideamic and antioxidant effects of Dihar, a polyherbal Ayurvedic formulation in streptozotocin induced diabetic rats. Indian Journal of Experimental Biology. 2009; 47:564-570.

38) Govindachari TR, Sathe SS, Vishwanathan N.Gentianine, an artifact in *Enicostemma littorale blume.* Indian J. chem.1966; 4:201-202.

39) Singh, A, Malhotra S, Subban R.Anti-inflammatory and Analgesic Agents from Indian Medicinal Plants. International Journal of Integrative Biology. 2008; 3(1): 57-72.

40) Ambikapathy V, Mahalingam R, Panneerselvam A.GC-MS Determination of Bioactive compounds of *Enicostemma littorale* (Blume). Asian Journal of Plant Science and Research. 2011;1(4): 56-60.

41) Prince PSM, Srinivasan M.*Enicostemma littorale* Blume aqueous extract improves the antioxidant status in alloxan diabetic rat tissues. Acta Poloniae Pharmaceutica - Drug Research.2005; 62 (5): 363-367.

42) Sathishkumar R, Lakshmi PTV, Annamalai A. Comparative analysis of Non-enzymatic and Enzymatic antioxidants of *Enicostemma littorale* Blume. International Journal of Pharma and Bio Sciences.2010;1(2): 1-16.

43) Praveena P, Sudarsanam D, Saravana K.GC, GC/ MS Characterization of the *Enicostemma littorale*. World Journal of Pharmaceutical Research.2014; 3(5): 844-852.

44) Vinotha S, Thabrew I, Sivapalan S. Standardization of Vellarugu Chooranam: A Siddha Herbal Drug. International Journal of Ayurveda and Pharma Research. 2014; 2(3): 44-53.

45) Vinotha Sanmugarajah. A Comparative Clinical Study on the Efficacy of *Amukkirai / Vellarugu chooranam* with *Thalangai ennai* in the Treatment of Knee Osteoarthritis. Doctor of Philosophy (Ph. D) Thesis. Faculty of Graduate Studies, University of Jaffna;2^{4th} April 2015.p.1-319.

46) KalaS, Jhonson M, Janakiraman N, Anto Arockiaraj A, Iyan Raj S, Bosco D.Pharmacognostic and phytochemical studies on some selected ethnomedicinal plants of Tamil nadu, South India. International Journal Med. Arom. Plants. 2011; 1(2): 89-94.

47) Sarwar M. *Enicostemma littorale* have Potential as Functional Food Ingredient. Research Journal of Medicinal Plant. 2012; 6(1): 4-5.

48) Anwar M, Ahmad M, Aslam M, Aftab K. *Enicostemma Littorale:* A New Source of Swertiamarin. Pakistan Journal of Pharmaceutical Sciences. 1996; 9(1):29-35.

49) Subasini U, Omprakashm NTV, Suneelkumar Alvin Jose M, Rajamanickam V. Phytochemical evaluation and hypocholesterolemic activity of *Enicostemma axillare.* Current Pharma Research. 2010;1(1): 30-35.

50) Gite VN, Pokharkar RD, Chopade VV, Takate SB. Evaluation of Physicochemical Standardization Parameters of *Enicostemma axillare*. J. Biosci Tech.2010a;1(4): 187-190.

51) Hariram SB, Deepika B, Manjubharathi N, Alamelu M, Chandran M. Phytochemical screening of different parts of plant *Enicostemma axillare* (Family – Gentianaceae). Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2011;2(3): 971.

52) Leelaprakash G, Dass SM. In-vitro Anti-Inflammatory activity of Methanol extract of *Enicostemma axillare.* International Journal of Drug Development & Research. 2011;3(3): 189-196.

53) Rana VS, Dhanani T, Kumar S. Improved and rapid HPLC-PDA method for identification and Quantification of swertiamarin in the aerial parts of *Enicostemma axillare*. Malaysian Journal of Pharmaceutical Sciences.2012;10(1):1–10.

54) Ramesh B, Dharaniyambigai K. Phytochemical screening and In-vitro antioxidant activities of aqueous extract of *Enicostemma littorale* Blume. International Research Journal of Biochemistry and Bioinformatics.2012;2(9): 200-204.

55) Sathishkumar R, Lakshmi PTV, Annamalai A.Estimation of Biomass contents and Phyto constituent analysis of *Enicostemma littorale* Blume. International Journal of Pharma and Bio Sciences. 2012; 3 (3):506 – 522.

56) Mathur R. Phytochemical and Antimicrobial Evaluation of Plant Extracts of *Enicostemma hyssopifolium*. Journal of Pharmacognosy and Phytochemistry. 2013; 2(4):30-36.

57) Vinotha S, Thabrew I, Sri Ranjani S.Phyto, Physicochemical Standardization of Medicinal Plant *Enicostemma Littorale* Blume. IOSR Journal of Pharmacy. 2013a; 3(2): 52-58.

58) Vinotha S, Thabrew I, Sri Ranjani S.Preliminary Phytochemical Screening of Different Extracts of Whole Plant of *Enicostemma littorale* Blume. International Journal of Sciences: Basic and Applied Research (IJSBAR). 2013b; 11(1): 99-104.

59) Abirami P, Gomathinayagam M. Biochemical composition of *Enicostemma littorale* Blume extracts. Bangladesh J. Bot. 2013;42(2): 367-369.

60) Selvaraj S, Chittibabu CV, Janarathanam B. Studies on Phytochemical screening, Antioxidant activity and Extraction of active compound (Swetiamarin) from leaf extract of *Enicostemma littorale*. Asian Journal of Pharmaceutical and Clinical Research. 2014; 7(4): 240-244.

61) Indumathi C, Durgadevi G, Nithyavani S, Gayathri PK. Estimation of terpenoid content and its antimicrobial property in *Enicostemma litorrale*. International Journal of Chem Tech Research, 2014;6(9): 4264-4267.

62) Ahamad J, Amin S, Showkat R Mir. Development and validation of HPLC-UV method for estimation of swertiamarin in *Enicostemma littorale*. Journal of Pharmaceutical and Bio Sciences. 2014; 1: 9-16.

63) Vigneswaran M, Prem Kumar G, Sivakumar S, Siva G, Nandakumaran T, Lakshmi Prabha A, Jayabalan N.A Compendious Review of *Enicostemma littorale* Blume. Panacea to Several Maladies. International Journal of Scientific & Engineering Research. 2017;8(6): 1817-1836.

64) Meshram PV, Moregaonkar SD, Gatne MM, Gaikwad RV, Zende RJ, Ingole SD, VanageGR. Physicochemical and Phytochemical Screening of Aqueous and Ethanolic Extracts of Costus Pictus D. Don and Enicostema Littorale Blum. Chemical Science Review and Letters.2017; 6(21): 426-434.

65) Selvam R, Muruganantham K, Subramanian S. Phytochemical Screening and Evaluation of in Vitro Antioxidant Efficacy of *Enicostemma littorale* Blume Leaves Extract. Int. J. Pharm. Sci. Rev. Res.2018; Article No. 18, 49(1): 113-120.

66) Nadkarni KM. Indian Materia Medica.Vol. 1. Bombay: Popular Prakashan Pvt. Ltd. 1st ed.1976.p. 485, 1184-1186.

67) Warrier PK, Nambiar VPK, Ramankutty C, Vaidyaratnam PSV. Indian Medicinal Plants.Vol. 2. Chennai: Orient Longman Ltd. 1st ed. 1997. p.374-375.

68) Kulkarni RR, Patki PS, Jog VP, Gandage SG, Patwardhan B. Treatment of osteoarthritis with a herbomineral formulation: a double-blind, placebo-controlled, cross-over study. Journal Ethnopharmacol. 1991; 33(1-2): 91-95.

69) Singh A. Phyto chemicals of Gentianaceae: A Review of Pharmacological properties. International Journal of Pharmaceutical Sciences & Nanotechnology. 2008;1(1):33-36.

70) Gupta S, Bhatt NM, Chauhan K, Pillai P, Pandya C, Thaikoottathil JV, Gupta SS. Protective Effect of *Enicostemma littorale* Blume Methanolic Extract on Gentamicin-Induced Nephrotoxicity in Rats. American Journal of Infectious Diseases. 2011; 7(4): 83-90.

71) Nampalliwar AR, Godatwar P.Anti-diabetic Activity of *Enicostemma littorale (Mamajjaka)* Leaf extracts in Streptozotocin Induced Diabetic Rats. International Journal of Ayuredic and Herbal Medicine.2012; 2(3): 541-547.

72) Shalini S, Swathi K, Mohan P, Swapna K, Ramesh babu P, Chandrika S. Anti-Epileptic Activity of *Enicostema Axillare* against MES and PTZ Induced Seizures in Rats. International Journal of Innovative Pharmaceutical Research.2011;2(1): 94-97.

73) Ramesh Babu P, Naga Priya KR. Antiepileptic activity of *Enicostema axillare* against MES and PTZ induced seizuresin Rats.International Journal of Innovative Pharmaceutical developments. 2013; 1(1): 88-92.

74) Dhanavanthy G, Jeyakumar S.Acute and Subchronic Toxicity Studies of Swertiamarin A lead Compound Isolated from *Enicostemma littorale Blume* in Wistar rats. Biosciences Biotechnology Research Asia. 2017; 14(1): 381-390.

75) Vijayvargia R, Kumar M, Gupta S.Hypoglycemic effect of aqueous extract of *Enicostemma littorale Blume (Chhota Chirayata)* on alloxan induced diabetic mellitus in rats. Indian Journal of Experimental Biology. 2000; 38: 781-784.

76) Maroo J, Vasu VT, Aalinkeel R, Gupta S.Glucose lowering effect of aqueous extract of *Enicostemma littorale Blume* in diabetes: a possible mechanism of action.J Ethnopharmacol. 2002; 81(3): 317-20.

77) Murali B, Upadhyaya UM, Goyal RK.Effect of chronic treatment with *Enicostemma littorale* innon-insulin-dependent diabetic (NIDDM) rats. Journal of Ethnopharmacology.2002; 81(2): 199-204.

78) Maroo J, Vasu VT, Gupta S.Dose dependent hypoglycemic effect of aqueous extract of *Enicostemma littorale Blume* in alloxan induced diabetic rats. Phytomedicine: International Journal of Phytotherapy & Phytopharmacology. 2003;10:196-199.

79) Srinivasan M, Padmanabhan M, Prince PSM, Effect of aqueous *Enicostemma littorale* Blume extract on key carbohydrate metabolic enzymes, lipid peroxides and antioxidants in alloxan-induced diabetic rats. Journal of Pharmacy and Pharmacology. 2005; 57(4): 497-503.

80) Showkat R. Mir, Javed Ahamad, Naila Hassan, Saima Amin.Swertiamarin Contributes to Glucose Homeostasis via Inhibition of Carbohydrate Metabolizing Enzymes. Journal of Natural Remedies.2016;16(4): 125-130.

81) Gopal RA, Gnanamani R, Udayakumar, Sadulla S.*Enicostemma littorale* blume-A potential hypolipidemic plant. Natural Product Radiance. 2004;3(6): 401-405.

82) Vihas T Vasu, Hiren Modi, Jyoti V. Thaikoottathil,Sarita Gupta,Hypolipidaemic and antioxidant effect of *Enicostemma littorale*Blume aqueous extract in cholesterol fed *rats*. Journal of Ethnopharmacology.2005;101(1–3):277-282.

83) Vasu VT, Modi H, Thaikoottathil JV, Gupta S.Hypolipidaemic and antioxidant effect of *Enicostemma littorale Blume* aqueous extract in cholesterol fed rats. Journal of Ethnopharmacology.2005; 101: 277–282.

84) Vaidya H, Rajani M, Sudarsanam V, Padh H,Goyal R.Cardiovascular Pharmacology Swertiamarin: A lead from Enicostemma littorale Blume for anti-hyperlipidaemic effect.European Journal of Pharmacology.2009; 617(1-3):108-112.

85) Thirumalai T, Viviyan TS, Elumalai EK, David E.Hypolipidaemic and antioxidant effect of Enicostemma littorale Blume.Asian Pac J Trop Biomed. 2011 Oct; 1(5): 381–385.

86) Vishwakarma SL, Goyalm RK.Hepatoprotective activity of Enicostemma littorale in CCl4 -induced liver damage. Journal of Natural Remedies. 2004; 4(2): 120-126.

87) Senthilkumar KTM, Rajkapoor B, Kavimani S. Protective Effect of *Enicostemma littorale* against CCl₄-Induced Hepatic Damage in Rats.Pharmaceutical Biology.2005, 43 (5):485-487.

88) Gopal RA, Udayakumar.Enzymatic and Non enzymatic Antioxidant activities of *Enicostema littorale* in p-DAB induced hepatocarcinoma in rats. In. J. of pharmacology.2008; 4(5): 369-375.

89) Baranisrinivasan P, Elumalai EK, Sivakumar C, Therasa SV, David E.Hepatoprotective effect of

Enicostemma littorale Blume and *Eclipta alba*during ethanol induced oxidative stress in albino rats. International Journal of Pharmacology. 2009;5(4): 268-272.

90) Gite VN, Pokharkar RD, Chopade VV, Takate SB,. Hepato-protective activity of *Enicostemma axillare* in carbon tetrachloride induced Hepato-toxicity in albino rats. International Research Journal. 2009;1(7): 3-5.

91) Jaishree V, Badami S, Krishnamurthy PT. Antioxidant and hepatoprotective effect of the ethyl acetate extract of *Enicostemma axillare* (Lam). Raynalagainst CCL_4- induced liver injury in rats. Indian Journal of Experimental Biology. 2010;48:896-904.

92) Jaishree V, Badami S.Antioxidant and hepatoprotective effect of swertiamarin from *Enicostemma axillare* against d-galactosamine induced acute liver damage in rats. Journal of Ethnopharmacology. 2010; 130:103–106.

93) Gite VN, Pokharkar RD, Takate SB.Hepato-protective activity of *Enicostemma axillare* in carbon tetrachloride induced Hepato-toxicity in albino rats. The Bioscan. 2010b; 5(1):109-111.

94) Gite VN, Pokharkar RD, Chopade VV, Takate SB. Hepato-protective activity of *Enicostemma axillare* in paracetamol induced hepato-toxicity in albino rats. International Journal of Pharmacy and Life Sciences.2010c; 1(2):50-53.

95) Srinivasan PB, Sreenivasan RS.Hepatoprotective Effect of *Enicostemma littorale* in Alcohol Induced Oxidative Stress in Male Albino Rats. International Journal of Pharmaceutical and Clinical Research.2011; 3(2):35-37.

96) Sadique J, Chandra T, Thenmozhi V, Elango V. The anti-inflammatory activity of *Enicostemma littorale* and *Mollugo cerviana.* Biochemical Medicine and Metabolic Biology.1987;37:167-176.

97) Sadique J, Chandra T, et al. The anti-inflammatory activity of *Enicostemma littorale* and *Mollugo cerviana.* J. Ethnopharmacol.2000;71(1-2):349-352.

98) Arivukkarasu R, Rajasekaran A, Murugesh S. Anti-inflammatory activity of alcoholic extract of *Adenema hyssopifolium* G.D on in acute & chronic experimental models in albino rats. Journal of Applied Biosciences. 2009; 19: 1049-1053.

99) Shivakumar SI,Shivakumar B,Jayachandran E, Suresh HM. Evaluation of anti-inflammatory activity of *Enicostemma littorale* Linn. Journal Biomed. 2009; 4(4):402-404.

100) Roy SP, Niranjan CM, Jyothi TM, Shankrayya MM, Vishawanath KM, Prabhu K, Gouda VA, Setty RS. Antiulcer and Anti-inflammatory Activity of Aerial Parts *Enicostemma littorale* Blume. Journal of Young Pharmacists.2010;2(4): 369–373.

101) Kanthasri A, Sheeba Rani M, Emmanuel S. Anti-inflammatory and Analgesic activity of *Enicostemma littorale* Blume using wistar rats. International Journal of Innovative Pharmaceutical Sciences and Research. 2014; 2(12): 2988-2993.

102) Shabi MM, Uthrapathy S, Raj CD, Krishnamoorthy G, Ravindhran D, Joseph J, Rajamanickam VG. Analgesic and Anti-Arthritic Effect of *Enicostemma littorale* Blume.Advances in Bioscience and Biotechnology.Scientific Research an Academic Publisher.2014;5(13): 1008-1024.

103) Anita Jain, Choudhary M, Katewa SS. Antimicrobial activity of *Enicostemma axillare* (Lam) Raynal. Journal of Pure and Applied Microbiology. April 2010; 4(1): 373-377.

104) Rita PM, Shailendra MB, Pramod PM, Dhananjay HM.Evaluation of in vitro antimicrobial activity of phytochemicals and extracts of Enicostemma littorale. Journal of Pure and Applied Microbiology.2010; 4(1): 379-385.

105) Gopal TK, Vidyadhar S, Saidulu M, Reddy UM, Chamundeeswari, Reddy LS, Saidulu A, Banji D.In-vitro antifungal activity of various extracts of *Enicostemma littorale.* IJPI's Journal of Biotechnology and Biotherapeutics.2011;1(2):24-30.

106) Praveena P, Sudarasanam D. in Vitro Antimicrobial Activity Studies on Enicostemma littorale (Lam), Raynal. whole plants. International Journal of Current Research. November 2011; 3(11): 123-124.

107) Pitchamuthu A, Muthiah G, Rajaram P.Preliminary study on the antimicrobial activity of Enicostemma *littorale* using different solvents.Asian Pacific Journal of Tropical Medicine. 2012;5(7): 552-555.

108) Thayalini T, Thevanesam V, Kathirgamanathar S, Gamage TM. Antibacterial Activity and Preliminary Screening of Phytochemicals of Whole Plant of *Enicostemma littorale*. Tropical Agricultural Research. Short Communication. 2012; 24(1): 99-105.

109) Shanmugapriya ON, Priya S.Antibacterial Activity of *Enicostemma Axillare* against Wound Pathogens. Research & Reviews: A Journal of Biotechnology. STM Journals. 2014;4(3): 1-3.

110) Lavanya B, Deepa Philip C. Invitro Antioxidant And Antibacterial Studies On Enicostemma Littorale Flower EXTRACT.World Journal of Pharmaceutical Research. 2015;4(11):1059-1066.

111) Patel DB, Rathod MC, Dhale DA.Bio-autography guided screening of antimicrobial compounds produce by Enicostemma littorale Blume. World

Journal of Pharmaceutical Sciences. 2015;3 (4): 749-753.

112)Mullai Nila K, Karthikeyan J.Phytochemical Profiling, Antibacterial Potential and GC-MS Analysis of Methanol Leaf Extract of *Enicostemma axillare*. Int. J. Curr. Microbiol. App. Sci. 2017; 6(7):2688-2695.

113)Kowsalya R, Vinoth A, Ramya S, Antibacterial activity of silver and zinc nanoparticles loaded with *Enicostemma Littorale*. Journal of Pharmacognosy and Phytochemistry. 2019; 2: 335-340.

114)Mishra S, Mishra A, Shukla P, Shukla P. In-Vitro Anthelmintic activity of *Enicostemma littorale* Blume. International Journal of Pharmaceutical Sciences and Research.2011; 2(5): 1193-1196.

115)Jaishree V, Badami S, Bhojraj S. In Vitro Antioxidant activity of *Enicostemma axillare.* Journal of Health Science. 2008; 54: 524-528.

116)Jaishree V, Badami S.Antiedematogenic and Free Radical Scavenging Activity *of* Swertiamarin Isolated from *Enicostemma axillare.* Pharmacology. Planta Med. 2009; 75(1): 12-17.

117)Gomathinayagam M, Abirami P, Panneerselvam R. Antioxidant activity of the medicinal plant *Enicostemma littorale* Blume. International Journal of Green Pharmacy. 2011; 5(4): 342-345.

118)Akhtar H, Antioxidant Potential of Dried *Enicostemma littorale,* Parkistan Journal of Biological Sciences, 2011, 14(20): 956-957.

119)Krishnaveni A, MohandassS. Anti-Oxidant Activity of *Enicostemma axillare* (in vitro studies). Journal of Pharmacy Research. 2012; 5(8):3954-3956.

120)Amit Vaibhav, Meera Antiwal, Jai Prakash Singh, Om Prakash Singh.Effect of *Enicostemma littorale* Blume *(Mamajjaka)* Therapy on Oxidant-Antioxidants levels in Metabolic Syndrome Patients*.* International Journal of Bio pharmaceutics. 2017;8(1): 33-37.

121)Vinotha S, Thabrew I, Sri Ranjani S. In-Vitro Antioxidant Activities of Aqueous and Methanol Extracts of *Enicostemma littorale* Blume. RA Journal of Applied Research. 2018; 04(4):1649-1655.

122)Bhatt NM, Barua S, Gupta S.Protective Effect of *Enicostemma littorale* Blume on Rat Model of Diabetic Neuropathy.American Journal of Infectious Diseases. 2009; 5(2): 99-105.

123)Sonawane RK, Vishwakarma SL, Lakshmi S, Rajani M, Padh M,Goyal RK. Amelioration of STZ-induced type 1 diabetic nephropathy by aqueous extract of *Enicostemma littorale* Blume and swertiamarin in rats. Molecular and Cellular Biochemistry.2010;340(1-2): 1-6.

124)Gohil TA, Patel JK, Vaghasiya JD, Manek.Anti-hyperglycemic and anti-hyperinsulinemic effect of aqueous extract of *Aegle marmelos* leaf and *Enicostemma littorale*. Ind. J Pharm. 2008; 40(2): 66–91.

125)Kavimani S, Manisenthilkumar KT. Effect of methanolic extract of *Enicostemma littorale* on Dalton's aseptic lymphoma. Journal of ethnopharmacol.2007;71:349-352.

126)Saravanana S, Prakash Babua N, Pandikumara P, Karunai Raj M, Gabriel Paulraja S, Ignacimuthua S. Immunomodulatory potential of *Enicostema axillare* (Lam.) A. Raynal, a traditional medicinal plant. Journal of Ethnopharmacology. 2012; 140: 239– 246.

127)Gupta S, Dadheech N, Singh A, Soni S, Bhonde RR. *Enicostemma littorale*: A new therapeutic target for islet neogenisis. International Journal of Integrative Biology. 2010; 9(1): 49-53.

128)Jaishree V, Badami S, Rupesk Kumar M, Tamizhamani T. Antinoceptive Activity of Swertiamarin Isolated from*Enicostemma axillare.*Phytomedicine. 2009; 16: 227-232.

129)DossVA, Dharaniyambigai K.Antidepressant activity of Enicostemma littorale blume in shp2 (protein tyrosine phosphatase)-inhibited animal model of depression. International Journal of Prevntive Medicine. 2016; 7(1): 112.

130)Shalini S, Saravana Kumar A. Effect of *Enicostema axillare* w.p Extract on Neurotransmitters concentrations in Rat brain after induction of seizures. International Journal of Experimental Pharmacology.2011; 1(1): 7-11.

131)Shalini S, Saravana Kumar A, Meenakshi Sundaram R. Effect of *Enicostema axillare* Extract on Antioxidant enzymes levels in rat brain after induction of Seizures. International Journal of Current Pharmaceutical & Clinical research. 2011;1(1):18-20.

132)Praveena P, Godse A, Pawar M, Kulkarni S, Sudarsanam D.In-Vitro Anti-HIV activity studies on *Enicostemma littorale* (Lam) Raynal*.* Whole plants. World Journal of Pharmaceutical. 2014a; 3(6): 1343-1352.

133)Jeyam M, Muthuselvi M, Sharanya M, Ramalakshmi Oviya I. In Vitro and In -Silico approach to evaluate the Anti-Dermatophytic activity of *Enicostemma littorale.* International research journal of Pharmacy.2013; 4(10): 78-83.

134)ShanmukhaI, Vinuth C, Manjusha MP.The Effect of *Enicostemma littorale* Blume on Adrenaline-Induced Hypertensive Rats. Journal of Pharmaceutical Research.2017; 16(3): 224-228.

135)Soni S, Gupta S.In-vitro Anti Plasmodial Activity of *Enicostemma littorale.* American Journal of Infectious Diseases. 2009; 5 (3): 259-262.

136)Jude Eokokon, Paul A Nwafor, Glory O Abia, Hermant K Bankhede.Antipyretic and antimalarial activities of crude leaf extract and fractions of *Enicostema littorale.* Asian Pacific Journal of Tropical Disease. 2012; 442-447.

137)Garg ankur, Singh Randhir. Anti-obesity activity of aqueous and ethanol extracts of *Enicostemma littorale* in high fat diet induced obese rats. International Journal of Phytomedicine**.** Oct. 2014;6(3): 433-443.

138)Ramaiyan Dhanapal, Vijaya Ratna J, Malaya Gupta, Sarathchandran I. Preliminary study on antifertility activity of *Enicostemma axillare* leaves and Urena lobata root used in Indian traditional folk medicine. Asian Pacific Journal of Tropical Medicine. 2012; 616-622.

139)Vishwakarma SL, Bagul MS, Rajani M, Goyal RK. A sensitive HPTLC method for estimation of swertiamarin in *Enicostemma littorale* blume, Swertiachirata (wall) Clarkeand in formulations containing *E. littorale*. J Plan Chromatogr. 2004; 17: 128-131.

140)Laxman S, Bala P, Kachwala Yusuf, Nancy P. Pharmacognostical Standardization of *Enicostemma littorale Blume*. Pharmacognosy Journal. November 2010;2(16): 12-20.

141)Alam P, Ali M, Singh R, Shakeel F.Estimation of Swertiamarin in *Enicostemma littorale* and Marketed Formulations Using HPLC-UV Method. Journal of Bioanalysis & Biomedicine.2009;1(1): 022-027.

142)W.H.O.Organization Mondiale De La Sante, Quality control methods,. World Health Organization, regional office for South-East Asia. Traditional hrerbal remedies for primary health care. India. 2010; 1-20.

143)Sane RT, Chawla JL, Kuber VV. Indian Drugs. 1997. 34; p. 580-584.

144)Shwetajain, Chanderachud Sharma, Pankaj Khatri, Atul Jain, Ankur Vaidya. Pharmacognostic and Phyto chemical Investigations of the Leaves of *Zizyphus xylopyrus* (Retz) Willd. International Journal of Pharmacy and Pharmaceutical Sciences. 2011;3(2): 122-125.

145)Swamy P, Mulla SK. Preliminary Pharmacognostical and Phytochemical Evaluation of*Portulaca quadrifida* Linn. International Journal of Pharm. Tech. Research. 2010;2(3):1699-1702.

146)Madhav NVS, Upadhyaya K, Bisht A. Phytochemical Screening and Standardization of Poly herbal formulation for Dyslipidemia. International Journal of Pharmacy and Pharmaceutical Sciences.2011;3(3): 235-238.

147)Pandey MK, Singh GN, Sharma RK, Lata S. Standardization of Yakrit Plihantak Churna: An Ayurvedic Poly herbal formulation.IJPSR. 2012; 3(1): 171-176.

148)William H, George WLJ. Official Methods of Analysis of AOAC International. 18th edition. 2005 (current through revision 2, 2007). Agricultural Chemicals; Contaminants; Drugs, Gaithersburg, Maryland, USA, AOAC Official method 986.15, 999.10 and 999.11; Chapter 9: p.1-22.

149)W.H.O. Basis Tests for Drugs, Pharmaceutical substances. Medicinal plant materials and Dosage forms. World health Organization. Geneva; 1998.p. 1-20.

150)Kunle OF, Egharevba HO, Ahmadu PO. Standardization of herbal medicines. A review. International journal of Bio diversity and Conservation. 2012;4: 101-112.

Cite this article as:
Vinotha Sanmugarajah. A Review on Therapeutic and Pharmacognostic Properties of Vellarugu (Enicostemma Littorale Blume). International Journal of Ayurveda and Pharma Research. 2020;8(4):47-67.
Source of support: Nil, Conflict of interest: None Declared

***Address for correspondence**
Dr. (Ms.)Vinotha Sanmugarajah,
Senior Lecturer,
Unit of Siddha Medicine,
University of Jaffna, Sri Lanka
Email: vsanmuga@univ.jfn.ac.lk
vsanmuga07@gmail.com