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Research Article

THE VOYAGE OF *TINOSPORA CORDIFOLIA* (GUDUCHI) FROM VEDIC TO MODERN ERA: A REVIEW

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ABSTRACT

Tinospora cordifolia (*Guduchi or Amrita*) is popularly known in the Indian system of medicine as Giloe and has been in traditional use for several centuries in the treatment of fever, leprosy, asthma, anorexia, jaundice, diabetes, chronic diarrhea & dysentery, gout, skin-infections, irritability of stomach etc. It is mentioned in Ayurvedic literature as a constituent of several *Ayurvedic* compound preparations like *Amritarista, Guduchyadi Modaka, Samsamani vati, Guduchyadi lauha, Pnachatikta ghrita* and *Balaguduchyadi taila* etc has been used in general debility, dyspepsia, fever, urinary diseases and skin diseases etc also. This paper presents an exploration of critical and comparative review on morphology, variety, chemical properties, therapeutic properties and their various uses from Vedic to Modern era.

KEY WARDS: *Tinospora chordifolia*, *Amrita, Ayurveda*, Gender instability, Morphology, Phytochemistry, Variety , Medicinal importance

INTRODUCTION

The world Health Organisation (WHO) reported that more than 80% of the world population trust on traditional medicine particularly on plant drug for their primary health care needs [1]. In India local empirical knowledge about medicinal properties of plants is the basis for their uses as a home remedies. Plants have been the base of many traditional medicines throughout the world for thousands of year and especially in India the science of *Ayurveda* has been continued to provide new remedies through these plant products to mankind. A research paper entitled "A Neanderthal flower burial in northern Iraq" published in the renowned journal named 'Science' in the year 1975 revealed that fossil studies have confirmed the use of plants 'a means of therapy' in the Middle Paleolithic age some 60,000 years ago[2]. This plant, *T. cordifolia*, occupies the top of the list of 'Ayurvedic Materia Medica' because of its extraordinary power of healing. Ayurveda, the traditional (ISM) is around 5000 years old healing tradition rooted in ancient Indian culture, designates this plant by the synonym '*Amrita*'. It is a Hindu mythological term that refers to the heavenly elixir that has saved celestial beings from old age and kept them eternally young.

The Medical tradition of *Ayurveda* is traceable to Vedas of which *Atharva Veda* is an important repository. *Atharva Veda* recommends charms drugs as well. It was only during the period of *Kauchika sutra*, the value of the herbs was more appreciated, through charms were also in vogue. The herb *Guduchi* being used as a medicament since vedic period. The word " *kudruchi*" is found in the text *kuchika sutra* which direct heir to *Atharvan* (*Aharv veda*) tradition with a touch

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of systematization and attempt at integration and application of both the traditions, i.e. the tradition of charms and meditational herbs[3].

DISTRIBUTION & MORPHOLOGY

Menispermaceae family consists of about 70 genera and 450 species [4]. *Guduchi* i.e. *Tinospora cordifolia* (willd) Mier ex Hook. F & Thorns is a large, glabrous, deciduous climbing shrub. The 40 species are distributed in tropical Africa, South-East Asia, Indo–Malaya region and Australia of which 3 species have been recorded from India. The species is widely distributed, extending from the Himalayas down to the southern part of peninsular India. According to Indian medicinal plant**,** the species which are used medicinally are *T. bakis* Miers - In Senegal, *T. Cordifolia* Miers, *T. crispa* Miers ,*T. malabarika* Miers - In Indo- China and *T. rumphii* Boerl - In Java. It is distributed throughout tropical Indian subcontinent and China, ascending to an altitude of 300 m. It is a fairly common wild plant of deciduous and dry forests of most distracts growing over hedges and small trees [5].

In relation to the synonyms of *Guduchi* as described in *Ayurveda* classics are co-relating to its botanical descriptions. Synonyms like *Amrutvalli, Amrutvallari, Amrutlata, Somvalli* and *Somalatika* refer to the fact that the plant is climbing on other tree. *Mandali, Kundali, Nagakumari* and *Tantrika* indicate that the plant grows on tree in a circular manner like as an young snake. *Chinna, Chinnaruha, Chinnudbhava* and *Chinnangi* refer to its capacity to grow even if it cut into pieces. *Madhuparni, Chadmika* and *Vatsadni* indicate the feature of its leaves. The leaves of the plant are like honey in taste. Calves eat the leaves. *Shyama* refers that the stem is brownish in colour and *Chakralakshana* refers to the circular ring- like or wheel-like appearances of its cross-section. Apart from the botanical description synonyms fall according to its therapeutic action also. Synonyms like *Amrita* i.e refers to nectar indicates that the person using this plant would live long and be healthy. *Jwaranasini* and *Jwarari*, these names indicate the specific use of this plant in fevers. The **stem** of *Tinospora cordifolia* is rather succulent with long filiform fleshy aerial roots from the branches with a thick, soft, warted, bark. The **bark** is creamy white to grey, deeply left spirally, the space in between being spotted with large rosette like lenticels. The leaves are membranous and cordate at the base. **Leaves** alternate, on long flexnose petioles, spreading 2-4 inches long, roundish - oval, entire, acute at the apex, quite smooth and thin. The leaves have bitter taste and an indistinct odour. When, the leaves seen in bulk they look intensely green. Mature leaves show yellowish to green colour. The flowers are small and yellow or greenish in colour. In auxiliary and terminal racemes or racemose panicles, the male flowers are clustered and female are usually solitary.The **Fruits** contain 3 or less. usually less by abortion shortly, stalked, subglobose drupes. The drupes are ovoid, glossy, succulent, red and pea sized. Flowers grow during the summer and Fruits during the winter and fruits are fleshy. The seeds are curved and single.

CLASSIFICATION

Inclusion of *Guduchi* in many groups which have specific and non specific therapeutic uses indicates the universality of its application from *Samhita* period of ancient classics. Under therapeutic consideration *Guduchi* has been classified in different *vargas* (groups). As it is being practiced medically it is brought under the heading of *ausadhi varga* (medicinal group)[6]. It is included under *saka varga* (vegitable group) as the climber along with it leaves which are used as vegetable. [7]. On the basis of morphological characters *Guduchi* is a twinner has been considered under *Vallipanchamula* [8]. As plant possesses *tikta rasa* (bitter taste) it included under *tikta skanda* [9] Due to *madhura vipaka* of plant it is included under *madhura skanda* [9]. On the basis of its therapeutic actions it is included under *dahaprasamana, vayasthapana, triptighna, trishnanigrahana, stanya sodhana, sirovirechana, rasayana*[9].

VARIETY

Guduchi and *Kanda Guduchi* depicted in ancient classics [10-12]. The commentary of *Bhavaprakash Nighantu* advocates the plant is available anywhere and is famous among climbing shrubs is two types *Valli Guduchi* and *Kanda Guduchi*. *Valli Guduchi*, which is taking support to climbing over other trees, when it becomes older in age the thickness of the stem, is equal to that of human arm. Its bark is paper-thin can easily separated. The leaves are similar to those of piper betle. Yellowish white coloured flowers which are in bunch cover the plant when the leaves fall, the fruit turn red when it ripens. *Kanda Guduchi* is also known as *Padma Guduchi*. It is not well known and easily available. Flowering type is same for both type. The leaves turn yellow and fall of 3-4 times in a year [13]

Under the consideration of phytomorphology, it is reported that Guduchi comes to pompous position as a delicious plant due to their sexual characters. Male and female plant of the Guduchi exhibit differences with physical forms in case of all parts as in stem, leaf, aerial and underground roots etc. Veination is looped in leaves of male plants while it being incomplete in leaves of female plants, which become the characters to identify them separately e. g. terminal marginal veination is looped in male plant unlike the female leaves where it is incomplete. can be distinguished prominently by inflorescence.

COMPARATIVE MORPHOLOGICAL CHARACTERS OF INFLORESCENCE [14]

Sl.No	Characters	Male Dominant Plant	Female Dominant Plant
	Inflorescence	Lax raceme, axillary or terminal	Same
	Flowers	Clustered in axils of small subulate bracts	Usually solitary
	Shape	Elongated, sepals 3 outer very small, ovate-oblong, acute, the inner larger, membranous, broadly elliptical, concave 0.3 - 0.5 cm; petals 6 equal about2 mm long, broadly spathulate, each loosely embracing a stamen, lamina subtrilobed, rhomboidal in shape, reflexed at apex, pistillode absent	Elongated, similar to male flower, margins of sepals reflexed, petals obovate not rhomboidal, 6 short and linear staminode
	Size	3.5 7.2 cm	6.2-16.57 cm
	Colour	Sepals and petals yellow	Sepals and petals comparatively greenish in colour

K.A.Geetha *et al* reported the gender instability phenomenon in the species i.e the temporary expression of bisexuality or hermaphrodism in males. According to report the species flowers profusely during November to May. In some of the male plants (24%), development of pistils started from February resulting in hermaphrodite flowers. In February within the male plants both staminate and hermaphrodite flowers are developed, however in different frequencies varying between 0 and 10% per inflorescence. All the male plants are converted to hermaphrodites by April and they gradually reverted to male starting from May. In the beginning of the conversion process, small protuberances appeared at the center of the staminate flowers producing no fruit set. At latter stage fully developed pistils are formed and fruits are developed. Fruit-setting are not successful in hermaphrodities (12%), especially in the initial month of sex conversion. Only one to two or three fruits are developed normally in sex converted flowers. However, in the case of females, the gender

expressions are highly stable and fruit-setting are success about 100% in pistils [15].

PHYTOCHEMISTRY

The discovery of active components from the plant and their biological function in disease control has led to active interest in the plant across the globe.

- Siddiqui (**1949**) investigated the stem and found three substances viz gilonin, a glycoside (m.p. 226 - 228^{0}C), gilenin a non-glycoside bitter (m.p. 210 - 212^{0}C) and gilosterol (m.p. 192 - 193^{0}C) [16]
- Patel *et al* (**1957**) while studying the trees and vegetable leaves observed that even dry sample of T.cordifolia contain crude protein and ash besides calcium, phosphate, carotene, ascorbic acid and other vitamins [17].
- Bhatt R.K (**1990**) has investigated structure of tinosporide. Its identity in all respects with jateorin (1s, 2s, 3r, 4r, 5r, 8s, 10r, 12s) -4-hydroxy-2, 3, 15-16diepoxycleroda 13(16), 14dieno-17 12,18 1- biscarbolactone [18].
- Akhila et al (**1992**) isolated the biosynthesis of the clerodanefurano-diterpene lactone skeleton in T cordifolia [19]

ACTIVE CHEMICAL CONSTITUENTS OF DIFFERENT PARTS OF *Tinospora cordifolia*

Active component types	Compound	Source	Reported biological effects in animal	In humans, cell lines	Reference
Alkaloids	Berberine,Choline, Palmatine, tembetarine, Magnoflorine, Tinosporine, Isocolumbin Tetrahydropalmatine Jatrorrhizine Aporphine alkaloids, N-formylasimilobine 2-O-β-D-glucopyranosyl-(1 →2)-β-D-glucopyranoside (tinoscorside A, 1) Aporphine alkaloids, N-acetylasimilobine 2-O-β-D-glucopyranosyl-(1 →2)-β-D-glucopyranoside (tinoscorside B, 2)	Stem, Root	Isoquinoline alkaloids have anti-cataract potential in rats. Anti-oxidant activity in mice, anti-cancer in ehrlich ascites carcinoma (EAC) mice, hypoglycemic activity in RINm5F rat insulinoma cell line	Anti-cancer, anti-viral infections, inflammation and immuno-modulatory roles. Neurological, psychiatric conditions, anti-diabetes	20 To 25
Glycosides	18-norclerodane glucoside, Furanoid diterpene glucoside, Tinocordiside, Tinocordifolioside Cordioside Palmatosides	Stem	Cytotoxic action, protection against iron-mediated lipid peroxidation of rat brain homogenate, anti-oxidant and hydroxyl radical scavenging activities in Swiss albino mice	Treats neurological disorders like ALS, Parkinsons', dementia, motor and cognitive deficits, and neuron loss in spine and hypothalamus. Immunomodulation: IgG increase and macrophage activation. Inhibits NF-κB and act as nitric oxide scavengers to show anti-cancer activities	26 To 35
Diterpenoid	Furanolactone, Clerodane	Whole	Chemopreventive potential in	Vasorelaxant: relaxes	

lactones	derivatives [(5R,10R)-4R-8R-dihydroxy-2S-3R: 15,16-diepoxy-cleroda-13 (16), 14-dieno-17,12S: 18,1S-dilactone] Tinosporides	plant	diethylnitrosamine (DEN) induced hepatocellular carcinoma (HCC) in rats	Norepinephrine induced contractions. Inhibits Ca++influx. Anti-inflammatory, anti-microbial, anti-hypertensive, anti-viral. Induce apoptosis in leukemia by activating caspase-3 and bax, inhibits bcl-2	36 To 41
Steroids	β-sitosterol, hydroxy ecdysone Ecdysterone Giloinsterol	StemsArial parts	Beta-Ecdysone shows anabolic and anti-osteoporotic effects in mammals	IgA neuropathy, glucocorticoid induced osteoporosis in early inflammatory arthritis, induce cell cycle arrest in G2/M phase and apoptosis through c-Myc suppression. Inhibits TNF-α, IL-1 β, IL-6 and COX-2. Activates NF-Kb	42 To 45
Sesquiterpenoid	Tinocordifolin	Stem			46
Aliphatic compounds	Octacosanol, Heptacosanol Nonacosan-15-one dichloromethane	Whole plant	Radiosensitizing activity in ehrlich ascites carcinoma mice. Modulating the pro-inflammatory cytokines. Inhibits proliferation of endothelial cells and Ehrlich ascites tumor cells	Anti-nociceptive and anti-inflammatory. Protection against 6-hydroxydopamine induced parkinsonism in rats. Down-regulate VEGF and inhibits TNF-α from binding to the DNA	23, 46 To 50
Miscellaneous compounds	3, (a,4-dihydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl) -tetrahydrofuran, Jatrorrhizine N-trans-feruloyl tyramine Giloin Tinosporic acid	Root whole plant	Insulin-mimicking and insulin-releasing effect. Enhanced phagocytic activity of milk polymorphonuclear cells in bovine subclinical mastitis	Protease inhibitors for HIV and drug resistant HIV. Tyramine is a neuro-modulator. Used to treat anxiety and depression by inactivating neurotransmitters	25, 51 To 55

NF-B=Nuclear factor-kappa-B, VEGF=Vascular endothelial cell growth factor, TNF=Tumor necrosis factor, IL=Interleukin, COX=Cyclooxygenase, ALS=Amyotrophic, Lateral Sclerosis, IgG=Immunoglobulin G, IgA=Immunoglobulin A

MEDICINAL IMPORTANCE

Refference of ancient classics reveals, *Guduchi* acts on human body through their *Rasapanchaka* (pharmacological action) i.e *Rasa*(taste)-*Tikta* (bitter), *Kasaya* (astringent), *Guna* (quality)-*Guru* (heavy), Snigdha (unctuous), *Virya* (action)-*Ushna (hot)*, *Vipaka* (post digestive effect)-*Madhur* (sweetness), *Doshghnata* (pacifying *dosa*)- *Tridosha Samaka* [56]

- *Pichu Dharana (medicated cotton to be set inside vagina)* of *Guduchyadi taila* in *vataja yoni vyapad* (vaginal diseases due to vitiation of *vata*) is very much help-full [57].

- Decoction made from *Guduchi*, *Tripahala (combination of Embelica officinalis,Terminalia chebula and* **Terminalia bellirica** (Gaertn.) Roxb) and *Danti* (*Baliospermum montanum* Wild) is used as *Dhara* or vaginal irrigation in *yonikandu* (vaginal Itiching). It is also effective in cystitis and spleenomegaly [58].
- Decoction used in malaria and chronic fever. Juice or powder with *takra* (whey) given in piles. *Piper longum* and honey mixed with decoction of *Guduchi* is much effective in chronic fever, spleenomegaly , cough and dyspepsia .Fresh juice is given in diabetes. Two or three drops of juice with powder of *pasanbhed* (*Bergenia ligulata*) with honey is effective in diabetes. *Guduchi* either with *Guggulu* (Comiphora mukul) or *Neem* or with *Haridra* (*Curcuma longa*), *Khadira* (*Acacia catechu*) and *Amalaki* (*Emblica officinalis*) is useful in almost all skin disease. Its oil triturated with milk is helpful in gout [59].
- Specific adjuvants are given with *Guduchi* for the treatment of vitiated *dosas* and diseases. *Guduchi* with *ghrita* (ghee), sugar, honey, jaggery, *eranda tail* (oil of *Ricinus comunis* Linn) and *sunthi* are beneficial for the vitiated *vata, pitta, kapha dosa*, constipation, gout and rheumatoid arthritis respectively [60].

PHARMACOGNOSY

1. Namjoshi A.N. *et al* (**1955**) have investigated the microphotographic reproduction of starches and have made comparative examination of *Guduchi Satwa* (starch) with commercial starches [61].
2. Mehra P.N *et al* (**1969**) have revealed that the market sample of *Guduchi Satwa* contains starchs from other sources rather than *Tinospora cordifolia*. The yield of Satwa was 0.4% with respect to fresh stem and 1.2% with respect of dry stem [62].
3. Bonde S.D. *et al* (**1989**) have studied wood anatomy of *Tinospora sinensis* (Lour) Merrill in relation with *T.cordifolia* Miers and added that *T.sinensis* is often mixed as adulterants or substitute for *T.cordifolia* [63].
4. Subbiah V.R. *et al* (**1990**) have reported that the aerial roots of *T.cordifolia* shows both gravitropic and phototropic response along with vascular difference and functions [64].

PHARMACOLOGY

- Gupta S S(**1964**) reported favorable influence of glucose tolerance was reported in rats by administering aqueous extract of *T cordifolia* for a month [65].
- Gupta S S (**1967**) have further carried out experimental evaluation of the drug for dissolution of urinary calculi in 22 rats, the stone formation was induced by implanting zinc pallets in the bladder. The deposition of the secondary salt over the zinc palates was inhibited by aqueous extract of *T. cordifolia.* In a further study reported that the drug not only relaxes smooth muscles of intestine and uterus but also inhibits constrictor response of histamine and acetyl choline on smooth muscles [66].
- Singh *et al* (**1974**) reported the water extract, produces marked but transit fall in blood pressure along with bradycardia and increases force of ventricular contraction in dog and dieresis in rats. It is significantly decreases blood urea levels in uremic dogs and patients [67].
- Anonymous (**1978**) reported the drug is to posses one fifth of the analgesic effect of sodium salicylate, its aqueous extract has a high phagocytic index. The active constituent in the drug was also found to inhibit in-vitro the growth of Mycobacterium tuberculosis [68].
- Pendse V.K. *et al* (**1981**) reported the dried stem of *T.cordifolia* (Miers) significantly inhibited carragenin induced odema as well as 5 Ht induced oedema in rats. It is also significantly antagonized formaldehyde induced oedema and decreased the excaudate formation in

granuloma pouch technique. In large doses it showed weak analgesic and antipyretic activity [69].

- Vedavethy *et al* (**1991**) have reported that the ethnol extracts of *T.cordifolia* exhibited significant antipyretic activity in experimental rats [70].
- Wadood N *et al* (**1992**) reported the aqueous, alcoholic, and chloroform extracts of the leaves of *Tinospora cordifolia* were administered in doses of 50, 100, 150 and 200 mg/kg body weight to normal and alloxan-diabetic rabbits. extracts of the leaves of *Tinospora cordifolia* have an insulin-like action and can significantly reduce the blood glucose but not the total lipid levels in normal rabbits and in alloxan-induced diabetic rabbits [71].
- Sharma D.N.K *et al* (**1995**) evaluated anti ulcer activity of *T. cordifolia*. The ethanol extract of the root of *T. cordifolia* administrated at a dose of 100mg/kg results protective action against stress induce ulceration. The activity was found to be compare to that of diazepam in experimental albino rats. The antiulcer activity has been reported as part of overall adoptogen active [72].
- Gagan *et al* (**1995**) have reported two new norditerpene furan glycoside (cordifoliside D cordifoliside E) were isolated as their tetra acetates from the polar butanol extract of *T. cordifolia* [73].
- Desai VR *et al* (**2002**) reported *Guduchi* extract was shown to inhibit the lipid peroxidation super oxide and hydroxyl radical in vitro. In another study it shows that dry stem crude extract contains a polygonal beta cell mitogen G1-4A which enhances immune response in mice [74].
- Bairy KL (**2004**) found Both the alcoholic and aqueous extracts of the root of *T cordifolia* produced decrease in learning scores in Hebb William naze and retention memory, indicating enhancement of learning and memory [75].
- Yin J *et al* (2008) Berberine an alkaloid obtained from the stem of *T cordifolia* has been shown to lower elevated blood glucose as effectively as metformin. Sharma et al 2012 confirmed the immunomodulatory activity of the polysaccharides of *T cordifolia* and also it was conclude that the polysaccharide with lowest sugar content showed highest activity and with highest sugar content showed lowest activity [76].

TOXICOLOGY

1. Peer F. *et al* (**1989**) have studied the efficacy of *T cordifolia* as a sole constituent in goats liver. Efficacy of Tc in experimental CCL4 result revealed hepato-protective action assessed through clinical and hematobiochemical improvement [77].
2. Zhao *et al* (**1991**) reported tubers of *T cordifolia* afforded a furanoid diterpene columbine. When tested in cell culture system columbin was non toxic to P388 and K.B. tumor cells. It did not show any antibacterial activity against E coli, S.aureus of Bacillus subtils at concentration up to 100 microg/ml. it was however active in brine shrimp toxicity test LC 50 3.2 microg/ml [78]
3. Concurrent jaily administration of *T cordifolia* stem and leaves extract prevent the toxic in fluencies of lead on haematological value and the results suggested that simultaneous supplementation of Tc protects against lead intoxication [79]

CULTIVATION

The plant is propagated by cuttings. It is perfectly suited to and grows well in almost any type of soil as well as under varying climatic conditions.

COLLECTION

The root and stem are collected in hot season when the bitter principle is most abundant and concentrated. For its *Satwa* (starch) preparation fresh stem should be collected at the flowering time when there is no leaves in the stem to get both qualitative and quantitative starch [13]

PARTS USED

The entire plant, stem, leaves and roots are used in medicines preferably more efficacious in fresh state.

SUBSTITUTE

T.cordifolia is a substitute for *Jivaka* (*Presumbly malaxis*).Where as substitute for *Guduchi* has not been mentioned in any of the classics of *Ayurveda*. However in practice fresh stem is efficacious than dry and is a good substitute for Columba.

ADULTERATION

The commonest species of *T.cordifolia* is likely to be adulterated are *T.sinensis, T.malabarica* and *T.crispa* are met with and often confused with each other.

CONCLUSION

The historical evidence confirms the use of this plant, the morphology based on synonyms of the species, the pharmacology and the therapeutic actions attributed to *T. cordifolia* from vedic to modern era have been validated by research scholars and scientist with modern evidences. So it is suggesting that this drug has immense potential and proves the acclaimed properties of *Rasayana* (rejuvenation).

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