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REVIEW ARTICLE

Immunomodulatory and Therapeutic Profile of *Tinospora Cordifolia* Linn. (*Guduchi*): A Phytopharmacological Review

Susmita D. Shedbale[1], Suhas Kumar Shetty[2], Pankaj Sharma[1]*, M. K. Mithraa[3]

[1]Post-Graduate Scholar, Department of Kayachikitsa, Rasayana evam Vajikarana Tantra, KAHERs Shri B.M. Kankanawadi Ayurveda Mahavidyalaya, PG Studies and Research Centre, Belagavi, Karnataka, India.
[2]Principal and Professor, Department of Kayachikitsa, KAHERs Shri B.M. Kankanawadi Ayurveda Mahavidyalaya, PG Studies and Research Centre, Belagavi, Karnataka, India.
[3]Post-Graduate Scholar, Department of Dravyaguna, Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan, Karnataka, India.

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ABSTRACT

With the prime motive of preventing, promoting health and curing, treating diseases, *Ayurveda* has been into preaching and practicing for ages. With the holistic approach of managing diseases, *Ayurveda* has its established way of dealing a *Vyadhi,* with nature-based medical products. *Guduchi*, *Tinospora cordifolia* Linn. Being such a medicinal herb has been in *Ayurvedic* clinical use for its immense potential to heal and promote health. *Ayurveda* classics as well as modern day researches have shown a wide spectrum of utility of *Guduchi. Guduchi* has been termed to be anti-hyperglycaemic, anti-oxidant, hepatoprotective, cardiovascular-protective, anti-allergic, anti-anxiety and stress, immunomodulatory, and many more. Since, *Guduchi* has a significant role in health preservation and treatment of diseases, this phytopharmacological review explores the immunomodulatory and therapeutic profile of *Tinospora Cordifolia* Linn. (*Guduchi*).

1. INTRODUCTION

Ayurveda, being the established system of medical science that evolved into a comprehensive health care management system, gives equal importance to maintenance, promotion of health by preventing ailments, and by curing them with nature-based medicines. Because of their active phytochemical constituents and miraculous curing properties, plants have been an integral part of Indian medicine for ages. *Tinospora cordifolia* Linn., commonly called *Guduchi* in Sanskrit and *Giloy* in Hindi, has gained widespread fame due to its immense application in the treatment of various ailments as per the classical *Ayurvedic* literature and pharmacological and medicinal functions due to several constituents such as alkaloids, glycosides, flavonoids, and terpenes. *Guduchi* has been proven in counteracting various disorders, its usage as anti-hyperglycaemic, anti-oxidant, hepatoprotective, cardiovascular-protective, anti-allergic, anti-stress, anti-malarial, immunomodulatory, anti-arthritic, anti-inflammatory, anti-neoplastic, anti-pyretic, antimicrobial, antiulcer, and a thrombolytic agent. Thus, the mention of *Guduchi* as "*Amrita*" in classical *Ayurveda* texts seems apt.

Corresponding Author:
Pankaj Sharma,
Post-Graduate Scholar, Department of Kayachikitsa, Rasayana evam Vajikarana Tantra, KAHERs Shri B.M. Kankanawadi Ayurveda Mahavidyalaya, PG Studies and Research Centre, Belagavi, Karnataka, India.
Email: ps214088@gmail.com

2. OBJECTIVE

The present write-up aims at exploring the role of *Guduchi* (*Tinospora cordifolia* Linn.) in health preservation and treatment of various ailments, backed by scientific research-based evidence.

3. METHODOLOGY

An in-depth literary study of the ancient treatises to discover the intricacies of *Guduchi* was done. Ayurvedic classics of *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya*, Textbooks of clinical and community medicine, scientific journals, Internet publications, and published literature available on PubMed and other scientific databases were consulted and reviewed for carrying out the present work.

3.1. Pharmacology of *Guduchi* (*Tinospora cordifolia* Linn.)

Guduchi, consists of dried, matured pieces of the stem of *Tinospora cordifolia* Linn., of *Menispermaceae* family, a perennial climber found

throughout tropical India. For regular collection drug is collected during the summer season, preferably in May. The drug is also used in its fresh form. Ayurvedic classics mentioned *Guduchi* as *Amritavalli*, *Amrita, Madhuparni*, *Guduchika*, *Chhinnobhava*, *Chhinnaruha,* and many other names. The major phytochemical constituents of this plant are terpenes, glycosides, alkaloids, steroids, aliphatic, and flavonoids.[1] Along with its chemical constituents, this plant is nutritionally due to the essential minerals present in its stem, namely, copper, calcium, phosphorus, iron, zinc, and manganese.[2] Berberine and lycopene are the two pigments that have been identified in its root, stem, and leaf.[3]

As per the Ayurvedic classical texts, the pharmacodynamic properties and actions of *Guduchi* are mentioned as follows:[5]

- *Rasa: Tikta*, *Kashaya*
- *Guna: Laghu*
- *Veerya: Ushna*
- *Vipaka: Madhura*
- *Karma: Tridosha Shamaka*, *Balya*, *Deepana*, *Rasayana*, *Sangrahi*, *Rakta Shodhaka*, *Jwaraghna.*

Dosage: 3–6 g of the drug in powder form, 20–30 mL of the drug for decoction [Figure 1].

3.2. *Guduchi* for Health and Diseases as per Ayurvedic Classics

On the basis of the pharmacodynamic properties of *Guduchi*, Ayurvedic classics described it on the basis of its *Karma* and *Gunas*. *Guduchi* has been mentioned at various stages in Ayurvedic classics for preventing health and management of disease conditions, as mentioned in Table 1.

For maintaining the health of an individual, various *Karmas* of *Guduchi* has been mentioned in the classics, such as *Tridoshahara*, *Amahara*, *Sangrahi*, *Hridya*, *Balya*, *Vatapitta Hara*, *Vahnikrita*, *Ayushya*, *Medhya*, *Medohara*, *Pittahara*, *Deepaniya*, and *Vayasthapana* that help an individual to attain the status of health and maintain it. The *Karmas* attributed to *Guduchi* as per the *Brihatrayee* are described in a comparative format in Table 2.

Furthermore, being a medicinal plant, the role of *Guduchi* has also been mentioned as per the context of the disease condition and its usage in the respective disease. Per say, *Guduchi* has been mentioned as *Kamalahara*, *Pramehaghna*, *Kandughna*, *Trishnanigrahana*, *Visarpaghna*, *Kasahara*, *Dahaprashamana*, *Kushthahara*, *Krimighna*, *Rakta-Arshoghna*, *Bhramahara*, *Chhardighna*, *Panduhara,* and *Jwarahara*. The use of *Guduchi* for treatment as per the *Brihatrayee* is summarized in Table 3.

For maintaining health and treatment of diseases, *Guduchi* has been used in different formulations or *Kalpanas* in the *Samhitas*. The commonly and widely used formulations of *Guduchi* are *Choorna* (e.g., *Rasayana Choorna*, *Sudarshana Choorna*); *Kashaya* (e.g., *Guduchyadi*, *Vasaguduchyadi*, *Manjishthadi*, *Punarnavashtaka Kashayam*); *Ghrita* (e.g., *Amritadi Ghrita*, *Panchtikta Ghrita*); Vati (e.g., *Guduchighana Vati*, *Chandraprabha Vati*); *Arishta (Amritarishta); Taila (Guduchyadi Tailam)* and *Rasa-Aushadhi* (e.g., *Chandrakala Rasa*, *Kamdugdha rasa*, *Gandhaka Rasayana*).

3.3. Research-based Evidence for *Guduchi* for Health and Diseases

A group of biologically active compounds, including alkaloids, diterpenoid lactones, glycosides, steroids, and aliphatic compounds has be isolated from *Tinospora cordifolia* Linn. plant. The biological activities of these major phytochemical constituents from different parts of *Tinospora cordifolia* are summarized in Table 4.

3.3.1. Immunomodulatory property

Guduchi has immunomodulatory effects due to stimulation of non-specific immune mechanisms, which is recorded due to the action of polysaccharides rich in glucose, fructose, and arabinose as monomer units.[15] *Tinospora cordifolia* extracts have been shown to result in up-regulation of interleukin (IL)-6 cytokine, resulting in acute reactions to injury, inflammation, activation of cytotoxic T cells, and B-cell differentiation.[16] A patent was granted for an ayurvedic composition of *Guduchi* used for prophylaxis and treatment of disorders like acquired immunodeficiency syndrome, flu, hepatitis, liver sclerosis, and TB through enhancing cellular and humoral immunity.[17] Furthermore, another patent was granted for an herbal combination containing *Guduchi* that decreased the amount of histamine in allergic cases.[18] Moreover, it was reported in a study that the macrophages induced an increased phagocytosis activity to non-infective microorganisms (Heat-killed yeast) and live infective microorganisms (*E. coli*) after *Guduchi* treatment by cytochemical parameters.[19] Hence, *Guduchi* has a strong immunomodulatory effect that could be utilised in multiple conditions of immunocompromised state.

3.3.2. Anti-diabetic property

Stem of *Guduchi* has been widely used for the therapy of diabetes for regulating the blood sugar in the traditional folk medicine in the Indian subcontinent. It has been reported to mediate its anti-diabetic potential through mitigating oxidative stress, promoting insulin secretion, and also by inhibiting gluconeogenesis and glycogenolysis, thereby regulating blood glucose.[20] Alkaloids, tannins, cardiac glycosides, flavonoids, saponins, and steroids, as the major phytoconstituents of *Tinospora cordifolia* Linn. have been reported to play an anti-diabetic role.[21]

3.3.3. Anti-inflammatory, analgesic, and antipyretic property

Guduchi has been used for centuries for the treatment of pain, fever, and inflammations. Analgesic action has been demonstrated to be due to both peripheral as well as a central mediated mechanisms.[22] Its anti-inflammatory effect has been noticed in the case of autoimmune arthritis as well mediated by a reduction in the synthesis of pro-inflammatory cytokines such as IL-1 beta, tumor necrosis factor-alpha, IL-17, and IL-17.[23]

3.3.4. Cardiovascular protective property

It is due to berberine present in this plant, which improves the vascular health by reducing endothelial inflammation.[24] Furthermore, in the case of disturbed lipid metabolism due to alcohol consumption, this plant was found to modulate lipid metabolism by inhibiting cholesterol and glucuronides.[25]

3.3.5. Hepatoprotective property

A study reported that the extract of *Tinospora cordifolia* Linn. is an important hepatoprotective agent, which may be because of several aspects, such as antioxidant as well as free radical scavenger properties, and induction of hepatic regeneration.[26]

3.3.6. Anti-oxidant property

The antioxidant property of this plant is due to an arabinogalactan polysaccharide and a phenolic compound.[27] The antioxidant property of its leaf extract powder is superior to its stem extract powder.[28] Its root extract provides protection from aflatoxin-induced nephrotoxicity due to the antioxidant activity of its alkaloid components. *Tinospora cordifolia* Linn. has the ability to scavenge free radicals generated during aflatoxicosis. *Tinospora cordifolia* Linn. Showed protection against aflatoxin-induced nephrotoxicity due to the presence of alkaloids such as choline, tinosporin, isocolumbin, palmatine, tetrahydropalmatine, and magnoflorine.[29]

3.3.7. Anti-microbial property

The anti-bacterial activity of *Tinospora cordifolia* Linn. extracts has been reported against *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Salmonella typhi*, *Shigella flexneri*, *Salmonella paratyphi*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Enterobacter aerogene*, and *Serratia marcesenses* (Gram-positive bacteria).[30]

3.3.8. Anti-toxic property

Tinospora cordifolia Linn. Extracts have been reported to scavenge free radicals in the body. The protective role of aqueous extract of stem and leaves of *Tinospora cordifolia* Linn. overcoming the toxic effects of lead, is shown as its effects on the haematological values.[31]

3.3.9. Anti-anxiety property

Furthermore, age-related decline in cognitive function is presented by memory loss, intellectual decline, and change in personality and behaviour is also slowed down by this herb, mainly by its anti-oxidant as well as dopaminergic activity.[32] It has anti-depressant activity by reducing monoamine oxidase (MAO) activity, thereby increasing the level of monoamines in the brain.[33]

3.3.10. Miscellaneous properties

Guduchi has endocrine system modulatory properties, antibiotic properties, anti-parasitic properties, anti-cancer properties, anti-hyperlipidemic properties, nephroprotective properties, radioprotective properties, thrombolytic properties, anti-diarrheal and anti-ulcer properties, osteoprotective properties, neuroprotective properties, and many more. A bird's eye overview on the medicinal and beneficial health applications of *Tinospora cordifolia* Linn. has been pictorially represented in Figure 2.

4. DISCUSSION

Tinospora cordifolia Linn. is commonly cultivated due to its excessive demand as it has importance in traditional Ayurvedic medicine, being used for ages in the management of fever, jaundice, chronic diarrhoea, cancer, dysentery, fracture, pain, asthma, skin disease, poisonous insect bites, snake bite, eye disorders, etc.[35] Even though all of its parts have some or other pharmacological action, its useful part is *Kaanda* (Stem). *Guduchi* is *Tridosha Shamaka* as it does *Vata Shamana* because of its *Ushna Virya* and *Madhura Vipaka*, *Pitta Shamana* due to its *Tikta*, *Kashaya Rasa,* and *Madhura Vipaka*, and does *Kapha Shamana* due to its *Tikta*, *Kashaya Rasa,* and *Ushna Virya*.

Guduchi possesses immunomodulatory effects due to the action of glycosides, which results in acute reactions to injury, inflammation, activation of T cells, and B cells. Cordifolioside A and syringin in *Guduchi* have been reported to have immunomodulatory activity. Patents have been issued for therapeutic approaches aimed at enhancing both cellular and humoral immune responses, as well as for strategies to mitigate histamine release in allergic conditions. *Guduchi* could be utilised in multiple conditions of an immunocompromised state. Its immunomodulatory and immunostimulatory effects make it a means of boosting the disease-fighting capability or the immunity of the individual. Alkaloids, tannins, cardiac glycosides, flavonoids, saponins, and steroids present in *Guduchi* have been reported to have anti diabetic properties. Phytochemicals present in *Guduchi* help in the reduction in synthesis of pro-inflammatory cytokines, making it an anti-inflammatory, analgesic, and anti-pyretic drug. Berberine present in *Guduchi* improves vascular health by reducing endothelial inflammation, explaining its cardiovascular protective property. Flavonoids, saponins, and tannins heli to modulate lipid metabolism.

Guduchi has the free radical scavenger property and protection against aflatoxin-induced nephrotoxicity due to the presence of alkaloids such as choline, tinosporin, isocolumbin, palmatine, tetrahydropalmatine, and magnoflorine confirms its anti-oxidant property. Due to its anti-oxidant and free radical scavenger property, *Guduchi* helps in the induction of hepatic regeneration, ensures its hepatoprotective activity. Studies have shown that it does not hamper the liver metabolism but, in turn, protect and decrease the metabolic damage and stress caused to the liver, heart, kidney, brain, etc. *Guduchi* have been reported to work against multiple gram-positive bacteria, proving its anti-microbial property. Due to its free radical scavenger, *Guduchi* overcomes the toxic effects of lead, leading to its anti-toxic property. *Guduchi* exhibits notable anti-depressant and anti-anxiety properties through the inhibition of MAO activity, resulting in elevated monoamine levels in the central nervous system. This aligns with its classification as a *Medhya Rasayana* drug as described by *Acharya Charaka*. In addition, various pharmacological attributes of *Guduchi* substantiate its appellation, *Amrita*, highlighting its potential therapeutic significance.

The pharmacological mechanism of action of *Guduchi* has been extensively assessed across various conditions; however, a comprehensive molecular-level investigation into the mechanisms and potential activities of this multipotent herb is currently in progress. Numerous studies have already been conducted, with many more in the pipeline, which will elucidate the intricate profiles of this extraordinary medicinal plant derived from Ayurvedic traditions.

5. CONCLUSION

By exploring the vast potential of this medicinal plant highlighted in Ayurveda classics, we can move away from burdening the body with harmful chemicals and instead embrace a safer alternative that promotes health and addresses diseases naturally. Furthermore, with its significant contributions to the realm of evidence-based medicine, *Guduchi* (*Tinospora cordifolia* Linn.) stands out as an exceptional resource.

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7. AUTHOR'S CONTRIBUTIONS

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Writing - Original Draft: PS, SDS
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This study does not require ethical approval as it is a review study.

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This is an original manuscript and all data are available for only review purposes from principal investigators.

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Table 1: Usage of *Guduchi* as per Ayurvedic texts

Classical text	Mention	References
Charaka Samhita[6]	*Sandhaneeya*	*C.Su. 4.5*
	Triptighna	*C. Su. 4.11*
	Stanya Shodhana	*C. Su. 4.18*
	Snehopaga	*C. Su. 4.21*
	Daha Prashamana	*C. Su. 4.41*
	Vaya Sthapana	*C. Su. 4.50*
	Madhura Skandha	*C. Vi. 8.139*
	Tikta Skandha	*C.Vi. 8.143*
	Shiro Virechana	*C.Vi. 8.151*
Sushruta Samhita[7]	*Vata Shamana Gana*	*S.Su. 37.7*
	Pitta Shamana Gana	*S.Su. 37.8*
	Shleshma Shamana Gana	*S.Su. 37.9*
	Shodhana Varga	*S.Su. 37.12*
	Ropana Varga	*S.Su. 37.24*
	Aragvadhadi Gana	*S.Su. 38.7*
	Shyamadi Gana	*S.Su. 38.29*
	Patoladi Gana	*S.Su. 38.33*
	Kakolyadi Gana	*S.Su. 38.35*
	Guduchyadi Gana	*S.Su. 38.50*
	Valli Panchamoola	*S.Su. 38.73*
	Shaka Varga	*S.Su. 46.270*
Ashtanga Hridayam[8]	*Shaka Varga*	*A.H.Su. 6.76*
	Padmakadi Varga	*A.H.Su. 15.12*
	Patoladi Gana	*A.H.Su. 15.15*
	Guduchyadi Gana	*A.H.Su. 15.16*
	Shyamadi Gana	*A.H.Su. 15.44*

Table 2: *Karmas* of *Guduchi* to maintain health as per *Brihatrayee*

S. No.	***Karmas* for *Swasthya Rakshana***	**Charaka Samhita**	**Sushruta Samhita**	**Ashtanga Hridayam**
1.	*Vatahara*	+	-	+
2.	*Amahara*	-	-	-
3.	*Sangrahi*	+	-	-
4.	*Hridya*	-	-	-
5.	*Balya*	+	+	+
6.	*Vahnikrita*	-	-	-
7.	*Vatapitta Hara*	+	+	-
8.	*Ayushya*	-	-	-
9.	*Medhya*	+	-	-
10.	*Medohara*	-	+	+
11.	*Pittahara*	+	+	+
12.	*Deepaniya*	+	+	+
13.	*Rasayana*	+	+	+
14.	*Tridosha Hara*	-	+	+
15.	*Vaya sthapana*	+	-	-
16.	*Rakta-doshahara*	-	+	+

Table 3: Use of Guduchi in treatment

S. No.	**Disease (*Rogaghnata*)**	***Charaka Samhita***	***Sushruta Samhita***	***Ashtanga Hridaya***
1.	*Kamala Hara*	-	-	-
2.	*Prameha Hara*	-	+	+
3.	*Kandughna*	+	+	+
4.	*Trishnanigrahana*	+	-	-
5.	*Visarpaghna*	-	-	-
6.	*Kasahara*	-	-	-
7.	*Dahaprashama*	+	+	+
8.	*Kushtahara*	+	+	+
9.	*Krimighna*	-	-	-
10.	*Rakta-Arshoghna*	-	-	-
11.	*Bhramahara*	-	-	-
12.	*Chhardighna*	-	+	+
13.	*Panduhara*	-	-	-
14.	*Jwaraghna*	+	+	+

Table 4: Biological activity of phytochemical constituents of *Tinospora cordifolia* Linn.

Phyto-chemical constituent	Derived from part	Biological activity in the human body
Alkaloids	Root and Stem	Anti-viral, anti-cancer, anti-diabetic, anti-inflammatory, neuro-protective, immunomodulatory, and psychiatric ailment.[9,10]
Diterpenoid lactones	Whole plant	Vaso-relaxant: relaxes norepinephrine-induced contractions, inhibits Ca2+influx, anti-inflammatory, anti-microbial, anti-hypertensive, anti-viral, induces apoptosis in leukaemia by activating caspase-3 and BAX.[11]
Glycoside	Stem	Treat neurological disorders (ALS, Parkinsonism, Dementia, motor and cognitive deficits) and neuron loss in spine and hypothalamus, Immunomodulation, Inhibits NF-kB and act as a nitric oxide scavenger to show anticancer activities.[12]
Steroids	Shoot	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, IL-6 and COX-2[13]
Aliphatic compounds	Whole plant	Anti-nociceptive and anti-6-hydroxydopamine induced parkinsonism in rats. Downregulates VEGF and inhibits TFN- α from binding to the DNA[14]

IL: Interleukin, TNF-α: Tumor necrosis factor alpha, VEGF: Vascular endothelial growth factor, NF-kB: Nuclear factor kappa B, ALS: Amyotrophic lateral sclerosis

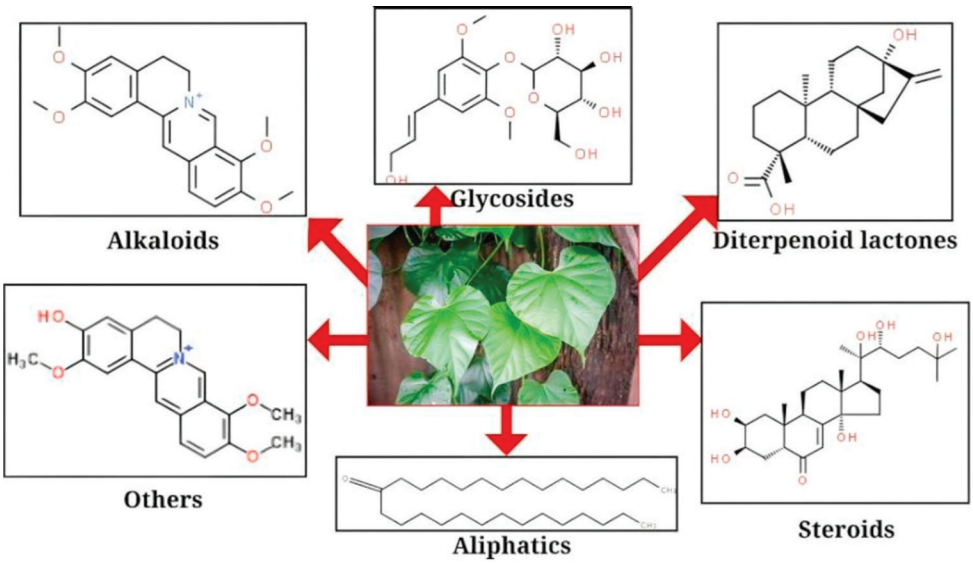

Figure 1: Active Compounds of *Tinospora Cordifolia* Linn.[4]

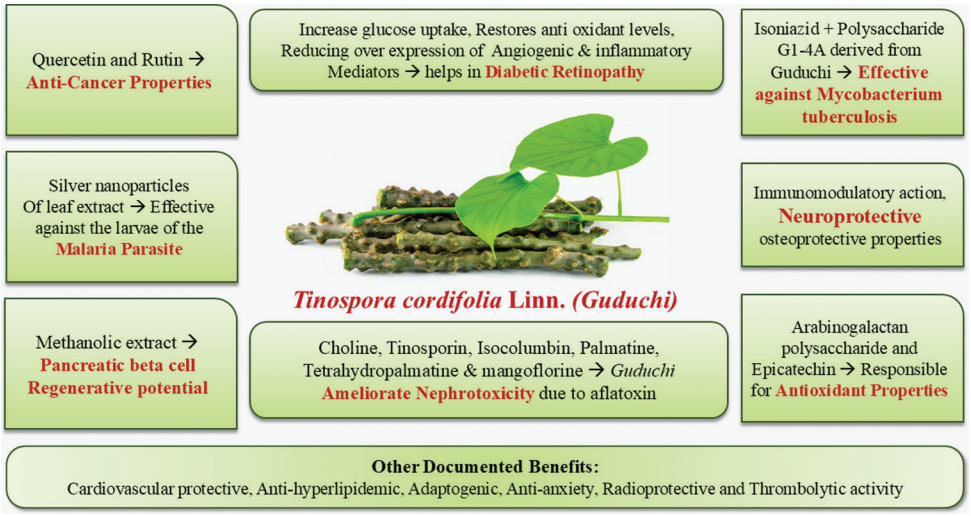

Figure 2: An overview of medicinal and health applications of *Guduchi*[34]