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## ROLE OF *TINOSPORA CORDIFOLIA* AS IMMUNE BOOSTER CURRENT COVID -19 PANDEMIC

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**ABSTRACT:** *Tinospora cordifolia* (Gulvel) is traditionally used in ayurvedic medicine for apparently much varied conditions. It is commonly used in combination with other substances or sometimes alone. Supportive evidence from pharmacological studies suggests its prominent role in immune-modulation in conditions like diabetes mellitus, obstructive jaundice, and hepatic and splenic injury. Antioxidant, radioprotective, antihyperglycemic, anti-inflammatory, antiulcer and antispasmodic properties and capacity to dissolve urinary calculi also have supportive evidence. It is a potential antidepressant and enhances cognition and memory. Immune-modulation, preventing oxidative damage, and relieving inflammation are likely explanations for benefits in infections, joint inflammation, and allergies. The constellation of various activities plays a role in its protective effects against antitubercular and cytotoxic drugs, and toxins. It is helpful in potentiating other substances in the form of simple extraction. This review discusses its formulations, the relevance of supportive evidence and possible mechanisms of actions for its claimed benefits, and future prospects.

**INTRODUCTION:** *Tinospora cordifolia* [*Tinospora cordifolia* (Wild) known as Gulvel or Guduchi, has been an extensively used and investigated plant from family Menispermaceae for its varied activities. It is a deciduous, fleshy, robust climber growing with support of mango or neem trees, and is also known as *Cocculus cordifolius* Dec, *Menispermum cordifolium* Wild and *Tinospora glabra* (N. Brum.) Merr<sup>1</sup>. Giloya, the plant's Hindi name, refers in Hindu mythology to a heavenly elixir used to stay off the aging and to stay young forever.

The Sanskrit name Guduchi means one that protects from illnesses. Hence, the word rejuvenator or adaptogen seem to be appeared in literature<sup>2</sup>. It is found in India, China, Myanmar, Sri Lanka, Thailand, Philippines, Indonesia, Malaysia, Borneo, Vietnam, Bangladesh, North Africa, West Africa, and South Africa.

In India, it is abundantly found in Maharashtra, Gujarat, Madhya Pradesh, Himachal Pradesh, and some other states in North and South India<sup>3, 4, 5, 6</sup>. In crude form, it is available in the market mostly as dried stem pieces. The present review discusses its formulations and methods of use. It searches the correlation of its traditional or claimed uses with possible mechanisms of action in light of evidence from modern pharmacologic studies and shows the link between the believed and the known. Throughout the present article, the plant is referred to as Gulvel or *Tinospora cordifolia* or *Tinospora*.

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**Names (Synonyms):** Gulvel, Giloe (English); Foon kan thang (Malaya); Makabuhay (Philippines); Brotowali, Andawali, Putrawali, Daun gade (Indonesia); and Boraphet, Wan kab hoi yai (Thailand)<sup>7, 8</sup>. Some names in Indian languages are Amrita, Amritvalli, Madhuparni, Giloe, Guduchi, Kundalini (Sanskrit); Giloya, Guduchi (Hindi); Ambarvel, Gharol, Gulvel (Marathi); Nimgilo, Gulancha, Palo (Bengali); Jivantik, Tippaatige (Telugu); Shindilakodi (Tamil); Ambrithu, Gulvel is an ayurvedic drug as per the Drugs and Cosmetic Act of India (1940). Its stem, leaves, fruits, and seeds have been mentioned to be useful; however, maximum activities are ascribed to its stem. Its taste is bitter, pungent, and astringent<sup>3</sup>. Ayurvedic pharmacodynamic properties for Rasa are Tikta (bitter) and Kashaya (astringent); for Guna are Lagh and Snigdha (light and oily); for Virya, it is Ushna (hot); and for Vipaka, it is Madhura (sweet). It has been called Tridosha-Shama means useful for alleviating all three doshas (Kafa Vata, and Pitta)<sup>6</sup>.

**Dosages and Mentioned Indications (Marketed Formulations):** Gulvel is available as tablets and syrups. Ayurvedic formulations like Amritarishta, Amrtottara kvatha churna, Guduci taila, Guduchyadi churna, Guduchyadi-kwatha, Guduchi sattva and Chinnodbhavadi kvatha churna have Gulvel as one of the constituents<sup>1</sup>. Some examples of strength and/or dosage and the mentioned indications include: 37.5 mg (for general debility, fatigue, old age, and as immunostimulant), 50 mg (antacid), 250 mg (menstrual disorders) in a combination<sup>9</sup>; 600 mg tablet twice daily (recurrent infections, to increase phagocytosis, anti-inflammatory, neutralizing toxins, chronic ear-nose-throat infections, stimulating growth of epithelial cells)<sup>10</sup>; 50 mg tablet twice daily in a combination (hematinic, hepatoprotective, bone marrow stimulant, antioxidant, and for alleviating degenerative processes in diabetes)10; 4, 20, 500 mg tablets (immune- modulator in infections, tuberculosis, malaria, diabetes and used with antimicrobials and nonsteroidal anti-inflammatory drugs)<sup>10</sup>; 200 mg tablet twice daily in a combination (rheumatoid arthritis)10; 300 mg tablet twice daily (hematinic, immune-modulator in chronic fever and infectious diseases)10; 3-6g (as powder) and 20-30 g (for decoction) as per Indian Herbal Pharmacopoeia<sup>11</sup>; 68.96 mg in a combination making a 500 mg tablet and 2 tablets

twice daily as Diabetes care tablet<sup>12</sup>; and 49 mg in combination making a 100 mg tablet, advised as 1 tablet twice daily for chronic recurrent ear-nose-throat infections<sup>13</sup>.

**Constituents and Nutritional Property:** Tinosporine, Tinosporaside, cordifolide, cordifol, and hepatacosanol are important constituents of Gulvel<sup>18</sup>. Barberine and palmatine are major alkaloids in stem. The glucosides are 18-norclerodane glucoside, sesquiterpenes like tinocordioside, tinocordifolioside, tinocordifolin, tinosponone, and cordioside, cordifolisides, and syringene<sup>1, 3</sup>. The stem contains immunologically active substances arabinogalactan and (1,4)-alpha-D-glucan<sup>19, 20</sup>. Crude values for food content in Gulvel include high fibre (15.9%), sufficient protein (4.5%-11.2%), sufficient carbohydrate (61.66%), and low fat (3.1%)<sup>21, 22</sup>. The nutritive value is 292.54 calories per 100 g<sup>21, 23</sup>. Gulvel has high potassium (0.845%) (Regulatory function of nerve impulse)<sup>21, 24</sup>, high chromium (0.006%) (Regulation of carbohydrate utilization and pathophysiological alternations in diabetes mellitus)<sup>25, 26</sup> sufficient iron (0.28%) (Hematopoietic functions)<sup>21, 27, 28</sup>, and sufficient calcium (0.131%) (Regulatory functions in blood coagulation, and nervous, cardiovascular, and musculoskeletal systems<sup>21, 29, 30</sup>.

**Traditional Uses:** These include general debility, fatigue, old age, hematinic, adaptogen, rejuvenator, and tonic and bleeding piles<sup>1</sup>; bleeding and menstrual disorders like metrorrhagia, postpartum hemorrhage<sup>31</sup> and as bone marrow stimulant<sup>1</sup>. Immune- modulation related claims include increasing phagocytosis, neutralizing toxins, stimulating the growth of epithelial cells, and supposed beneficial effects in recurrent infections, chronic fever, tuberculosis, malaria, diabetes, chronic ear-nose-throat infections and as an adjuvant with antimicrobials or nonsteroidal anti-inflammatory drugs<sup>10, 13</sup> and to relieve itching<sup>1</sup>. Genitourinary conditions include Mutrakriccha (urinary trouble) used alone or in combinations; and spermatorrhea, phosphaturia, dysuria, gonorrhoea, chronic cystitis, treatment and prevention of urinary calculi, incontinence of urine, to decrease the elevated blood urea concentration<sup>32</sup>, diuretic<sup>33</sup> and to treat impotence<sup>31</sup>. Inflammation, pain, and fever-related claims

include rheumatoid arthritis and gout<sup>3, 10</sup> and pain<sup>33</sup> and fever<sup>1, 31</sup>. Uses for antioxidant effect include alleviating degenerative processes in diabetes<sup>10</sup>, and for free radical-mediated injury, liver damage, jaundice, stress, and cancer<sup>33</sup>. Gastrointestinal claims include use as an antacid, carminative (dyspepsia, nausea)<sup>1, 31, 34</sup> and protective<sup>33</sup>. Hypoglycemic properties (apart from immune-modulation and antioxidant properties) relate to its supposed use in diabetes<sup>1, 33</sup>. Claims include antimicrobial and antihelminthic uses<sup>1</sup>. Gulvel has been claimed to be useful as a medium of Shodhan-Vidhil<sup>35, 36</sup> (to increase the effect of other substances like Guggul). Claims include erysipelas, ulcers, leprosy, snake bite, and scorpion bite<sup>18, 37, 38, 39</sup>.

### Mechanisms of Action Immune-modulation:

Immune-modulation by Gulvel has been established in obstructive jaundice, tuberculosis, and cancer in human and animal studies<sup>40-48</sup> and cordial, isolated from Gulvel showed inhibition of C3-convertase in the classic complement pathway, enhancement of humoral and cell-mediated immunity, increased IgG antibodies, and increase in granulocyte-macrophage colony-forming units. Macrophage activation by cordioside, cordiofolioside, and cordiol isolated from Gulvel, led to leucocytosis and enhanced neutrophil function<sup>49</sup>. Protective effects of Gulvel in *Escherichia coli*-induced peritonitis in mice showed improved phagocytic capacities of neutrophils. Cholestasis-induced immunosuppression in rats was significantly improved by Gulvel, suggesting its role as an immunomodulator in obstructive jaundice<sup>46, 50</sup>. Immunologically active substances, arabinogalactan<sup>19</sup>, and the novel (1,4)-alpha-D-glucan derived from Gulvel were shown to activate immune system through macrophage activation via toll-like receptor-6 (TLR6) signaling, nuclear factor kappa B (NF- kappa-B) translocation, and cytokine production<sup>20, 51</sup>.

The antiangiogenic activity was shown through the elevation of interleukin-2 (IL-2) and tissue inhibitor of metalloprotease-1 (TIMP-1)<sup>52</sup>. Immune-modulatory effects have implications in liver damage due to tuberculosis and anti-tuberculosis drugs, cancers and anticancer drugs, and malaria. Immune-modulation is also a likely basis for its claimed use as bone marrow stimulant, hematinic,

tonic or rejuvenator, and the supposed beneficial effects in general debility and old age<sup>1</sup>, due to additional antioxidant property. Supposed uses for prevention and management of recurrent infections including ear-nose-throat infections and symptomatic treatment of pruritus<sup>10</sup> also are related to immune-modulation.

### Plant Profile:

#### *Tinospora cordifolia*:



FIG. 1: GULVEL

### Plant Profile:

Family	Menispermaceae
Ayurvedic name	Amrita, Guduchi
Unani name	Giloe
Hindi name	Giloe, Gurcha
Trade name	Giloe
Parts used	Stem, root, whole plant

### Morphological Characteristics:

- Gurcha is a gregarious glabrous, twiner.
- Older stems are up to 2 cm in diameter and have corky bark.
- Aerial roots arise from nodal scars of branches.
- Stem and branches are specked with white vertical lenticels.
- Bark is grey-brown or creamy white, warty, papery thin, and peels off easily.
- Leaves are 5–15 cm, ovate, and acute.
- They are membranous when young but become more or less leathery with age.



FIG. 2: DRIED STEM OF GULVEL

**Hepatoprotective Properties:** Gulvel was shown to be protective against liver damage induced by carbon tetrachloride<sup>53</sup>, antitubercular drugs<sup>42, 43</sup>, bile salts<sup>54</sup>, in obstructive jaundice<sup>44, 46</sup>, and gamma radiation<sup>55</sup>. *In-vitro* inactivation of hepatitis B and E surface antigens<sup>56</sup>, and modifying Kupffer cell activity was demonstrated<sup>45</sup>. Protective effects extended to improvement in splenomegaly during chloroquine treatment of malaria<sup>57</sup>. Radioprotection was shown by a recovery in spleen weight, decreased apoptosis and DNA fragmentation, increased splenocyte number, macrophage adherence, interleukin-1(IL-1) beta, and granulocyte-macrophage colony-stimulating factor (GM-CSF)<sup>55</sup>.

**Antioxidant Property:** Phenolic compounds in Gulvel are antioxidants<sup>58, 59</sup>. *In-vitro* models showed nitric oxide and superoxide radical scavenging, inhibition of lipid peroxidation, reduction of ferric ions, and total antioxidant capacity<sup>4</sup>. It reduced superoxide and hydroxyl radical generation and the toxicity induced by free radicals. Alleviation of toxic effects of cyclophosphamide in mice was evident by total white blood cell counts, bone marrow cellularity, and esterase-positive cells. It partially reduced elevated lipid peroxides in serum and liver, and serum alkaline phosphatase and serum glutamic-pyruvic transaminase(SGPT)<sup>60, 61</sup>. Its role in preventing oxidative stress associated with infections was suggested with reference to catalase, glutathione-S-transferase, glutathione peroxidase, glutathione reductase, superoxide dismutase, and polyphenoloxidase<sup>62</sup>. These effects (along with immune-modulation) partially justify claims of

benefit in general debility, fatigue, old age, and as hematinic, rejuvenator, tonic, and effects in chronic recurrent infections<sup>58, 59</sup>.

**Anticancer Activity:** Anticancer actions of a formulation containing *Tinospora cordifolia*, *Asparagus racemosus*, *Withania somnifera*, and *Picrorrhiza kurroo* were shown in mouse macrophages<sup>63, 64</sup>. Effects related to modulation of chemotaxis, interleukin-1(IL-1), and tumor necrosis factor in ochratoxin-treated macrophages. Aqueous, methanolic, and dichloromethane extracts of Gulvel showed dose-dependent increases in lethality to HeLa cells (maximum activity with dichloromethane extract)<sup>65</sup>. Effects were related mainly to immune-modulatory functions. Antioxidant property also correlates with the amelioration of cyclophosphamide toxicity<sup>60, 61</sup>.

**Antidiabetic Activity:** Hypoglycemic activity of Gulvel was shown in alloxan-diabetic rats<sup>66</sup>. The aqueous and alcoholic extracts reduced fasting blood sugar and improved glucose tolerance, followed by deterioration after one month of treatment. Significant hypoglycemic effects were shown in rabbits treated with aqueous, alcoholic, and chloroform extracts of Gulvel leaves. The aqueous root extract of Gulvel caused a significant reduction in blood glucose, brain lipids, and hepatic glucose-6-phosphatase, serum acid phosphatase, alkaline phosphatase, and lactate dehydrogenase, and increased the body weight, hemoglobin, and hepatic hexokinase levels<sup>1, 67</sup>. An indirect action of Gulvel on carbohydrate metabolism was suggested through its favorable effect on endogenous insulin secretion and glucose uptake, and inhibition of peripheral glucose release<sup>68, 69</sup>. Amelioration of experimental diabetic neuropathy and gastropathy in rats and modulation of morphology and some gluconeogenic enzymes in diabetic rat kidneys suggest potential for preventing the complications of diabetes<sup>70, 71</sup>.

**Anti-inflammatory Action:** Extensive animal studies with aqueous and alcoholic extracts of Gulvel in acute and subacute inflammation using models of carrageenin-induced hind paw edema, induced edema and arthritis, adjuvant-induced arthritis, cotton pellet granuloma, and formalin-induced arthritis, and a clinical trial in rheumatoid arthritis showed its anti-inflammatory action<sup>72, 73</sup>.

<sup>74, 75, 76</sup>. Effect comparable to indomethacin was demonstrated, and a mechanism of action similar to nonsteroidal anti-inflammatory drugs was suggested <sup>73, 74, 75, 77</sup>.

Significant peripheral analgesic activity of Gulvel was shown by Randall-Selitto assay in rats and acetic acid-induced writhing test in mice. Although potentiation of morphine analgesia was demonstrated, a central analgesic effect was not observed on the tail clip and hot plate tests in mice <sup>1, 31</sup>. Antipyretic activity of ethanolic extract, hexane soluble preparation, and chloroform soluble portions Gulvel stem showed antipyretic activity on experimental evaluation in rats <sup>31</sup>.

These studies support the anti-inflammatory activity of Gulvel, relating to its mechanism of action similar to nonsteroidal anti-inflammatory drugs <sup>76, 77</sup>. Since central analgesia was not demonstrated, the suggested analgesic uses of Gulvel seem to correlate with peripheral analgesic activity to relieve the pain associated with inflammation <sup>75</sup>. This evidence supports the claimed uses in rheumatoid arthritis and gout <sup>32</sup>.

**Antistress Activity:** Gulvel has supportive evidence of normalization of stress-induced biochemical changes in norepinephrine, dopamine, and 5-hydroxytryptamine in experimental rat models and improved levels of 5-hydroxyindoleacetic acid (5- HIAA) (a metabolite of 5-hydroxytryptamine) in mice with ethanolic roots extracts<sup>85</sup>. Depression is characterized by decreased brain levels of monoamines like norepinephrine, serotonin, and dopamine. Established antidepressants act by inhibiting reuptake or breakdown of these amines and increasing their levels at postsynaptic receptors.

Antidepressant-like effect Gulvel was significantly reversed on tail suppression test by pretreatment of animals with prazosin (an alpha-1 adrenoceptor antagonist), sulpiride (a selective dopamine D2-receptor antagonist), p- chlorophenyl alanine (PCPA - a serotonin synthesis inhibitor), and baclofen (GABA- B agonist).

Inhibition of the metabolism of monoamines, particularly serotonin and noradrenaline, was also demonstrated. Hence the mechanism of antistress and antidepressant activities of Gulvel relates to

interaction with alpha-1 adrenergic, dopaminergic (D2), serotonergic, and GABA-B receptors leading to increased levels of norepinephrine, dopamine, serotonin, and gamma-aminobutyric acid (GABA).

Potentiation of brain monoamines by inhibition of monoamine oxidase is another suggested mechanism. GABA-B receptor antagonism is suggested as a basis for the development of novel antidepressants. Barberine, an alkaloid in Gulvel has been reported to have an antidepressant effect, and hence barberine seems to be an active component playing a role in the antidepressant effect of Gulvel.

Gulvel is mentioned as a medhya rasayana (learning and memory enhancer) and for bhrama (vertigo) in Ayurveda. Significant response to Gulvel was reported in children with moderate degree of behavioral disorders and mental deficit, with improvement in intelligence quotient levels. In a 21-day randomized double-blind placebo-controlled study, pure aqueous root extract enhanced verbal learning and logical memory.

Gulvel was shown to enhance cognition and memory in normal rats and reverse cyclosporine-induced memory deficit. Alcoholic and aqueous extracts produced a decrease in learning scores in Hebb-William maze and retention memory, with the protection of hippocampal neurodegenerative changes on histopathological examination in cyclosporine-treated rats.

**Genitourinary System and Reproductive System:** Experimental evaluation showed the benefits of *Tinospora* for dissolving urinary calculi. In rats and in human volunteers, it had diuretic effect comparable to hydrochlorothiazide. Decreased weight of testes, epididymis, seminal vesicles, and ventral prostate was demonstrated in male rats, a potential for antifertility activity. Uses for dissolving urinary calculi, as a diuretic and for decreasing blood urea concentration in uremia are thus substantiated.

Benefit in urinary tract infections does not have evidence of direct antibacterial action and is likely to have a correlation with its anti-inflammatory and immune-modulating activities. Supposed use to treat impotence does not correlate with the

apparently opposite finding of antifertility action seen in male rats<sup>31</sup>.

**Infections:** Gulvel is claimed to be useful in various infective conditions<sup>1, 10, 13, 78, 79</sup>, and tuberculosis. It has no specific antibacterial activity against *E. coli*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, or *Proteus vulgaris*<sup>14, 50</sup>. There seems to be insufficient evidence for its direct antimicrobial activity. The mechanism that plays a role in infections is the protective effect by immune-modulation, including effects on polymorphonuclear cells, phagocytes, and macrophage function<sup>46, 49, 50</sup>.

Another mechanism involves its antioxidant property, which is beneficial in decreasing oxidative stress and damage related to infections<sup>61</sup>. Use in infective diarrhea does not seem to involve antibacterial properties against any of the common enteric pathogens (*Salmonella*, *Escherichia coli*, *Shigella*, *Proteus* or *Pseudomonas*), but more of antispasmodic effect<sup>14, 35, 36</sup>.

Benefits in urinary tract infections do not have supportive evidence of direct antimicrobial activity and may be related to pain relief by dissolving urinary calculi, alkalization of urine, and immune-modulation. Similarly, there is no sufficient evidence of direct antimicrobial activity in tuberculosis; however, its use in tuberculosis relates to immune-modulation<sup>40</sup>, and preventing hepatotoxicity of antitubercular drugs<sup>42, 43</sup>.

Claims for usefulness in viral infections do not have supportive evidence from pharmacologic studies. There was evidence of clinical and symptomatic benefits in fungal otitis externa, chronic sinusitis, chronic tonsillitis, and chronic suppurative otitis media<sup>13</sup>.

In the absence of proven antimicrobial activity; immune-modulation, and antioxidant and anti-inflammatory action is the likely mechanism involved.

**Skin Disorders and Leprosy:** Traditional use of Gulvel has been mentioned in skin diseases<sup>38, 39</sup>. In Ayurveda, it has been mentioned as Kushtahara (means, useful in leprosy) and useful in skin disorders like Kandu and Visarpa. Gulvel has been

shown to have beneficial antileprotic activity in a combination formulation.

**Bronchial Asthma:** Gulvel stem aqueous extract decreased bronchospasm in guinea pigs, capillary permeability in mice and reduced number of disrupted mast cells in rats. Immune-modulation is also likely to be a response mechanism in allergies and bronchial asthma.

**Snake Bite:** Use has been mentioned in snake bite and scorpion bite due to its ability to remove exogenous and endogenous toxins<sup>18, 37</sup>. The most likely mechanism relates to immune-modulation and antioxidant properties.

**Osteoprotection:** Slower bone loss in tibia than that in controls was demonstrated in rats treated with Gulvel, showing potential for osteoprotective activity. Serum osteocalcin and cross-laps levels were significantly reduced. This suggested its potential use as an anti-osteoporotic agent.

**Seizures and Convulsions:** In comparison with phenytoin, ethanolic extract of Gulvel showed 61.1 percent inhibition of electroshock seizures in rats. Another report shows a lack of significant anticonvulsant activity during maximum electroshock and chemo shock tests in mice<sup>1</sup>. The link between claims and evidence: the believed and the known Evidences from various pharmacological studies suggest many overlapping mechanisms of actions likely to contribute to the beneficial effects of *Tinospora cordifolia* (Gulvel).

Immune-modulation, protective actions, and antioxidant properties seem to contribute profoundly to diabetes, obstructive jaundice, malaria, hepatic and splenic injury, protection from allergens and toxins, infections, inflammation, rheumatoid arthritis, gout, leprosy, and in preventing adverse effects of anticancer and anti-tuberculosis agents<sup>41, 42, 44, 46, 57, 60, 61, 64, 65</sup>.

The role of its antioxidant properties<sup>60, 62</sup> in degenerative diseases can serve as a potential area for further work. In addition to immune-modulation and hypoglycemic activity, high chromium content and protective effects in preventing complications of diabetes (neuropathy, nephropathy, and gastropathy) are remarkable<sup>66, 67, 68, 70, 71</sup>. Exploring these areas and search for the possibility of its

insulin-sensitizing and insulin secretagogue effect will help further to establish its status in the management of diabetes. Antidepressant effects of Gulvel by various mechanisms directed towards concentrating and potentiating brain amines (norepinephrine, dopamine and serotonin) have been a remarkable novel finding. Increased amine levels in the brain and preventing the breakdown of amines by inhibiting monoamine oxidase were the two important pieces of evidence.

Monoamine oxidase inhibitors were the older and comparatively more toxic antidepressants, whereas the selective serotonin reuptake inhibitors (SSRI) are the antidepressants of the modern era with fewer adverse effects. Since Gulvel has not been mentioned to be a highly toxic substance, it will be relevant to search if it has effects similar to the SSRI.

Antistress activity and improved learning and memory are potential directions for further research. *Tinospora* is shown to have an anti-inflammatory effect similar to nonsteroidal anti-inflammatory drugs, justifying its benefits in rheumatoid arthritis and gout<sup>74, 75, 77</sup> however, there is no evidence of specific activity directed against uric acid synthesis or excretion. Benefits are related to relief of inflammation and associated pain and immune-modulation.

It is remarkable that despite having a mechanism like nonsteroidal anti-inflammatory drugs (NSAIDs), it has antiulcer activity. This finding may provide Gulvel a status better than traditional NSAIDs (which precipitate peptic ulcers).

There is a potential for further work to search if it has any specific properties like celecoxib, of selectively inhibiting cyclooxygenase-2 (COX-2) enzyme secreted at sites of inflammation (without inhibiting COX-1 in the stomach). This shall help to clarify the gastric mucosal protection offered by Gulvel. In addition, its antispasmodic action is thought to involve possible histamine receptor (H2) blockade and muscarinic blockade.

It will be interesting to explore if it provides protection against peptic ulcers by similar mechanisms. Obviously, a potential exists for verifying its status in the treatment of peptic ulcer. There is no evidence for direct antimicrobial

activity of Gulvel<sup>14, 49, 50</sup>. Immune-modulation, protective action against allergens and toxins, and preventing oxidative stress related to infections work as contributory mechanisms for beneficial effects in infections.

These conditions include acute or chronic and recurrent infections of respiratory, urinary, and gastrointestinal tracts. Dissolving urinary calculi serves as an additional mechanism in related urinary infections and dysuria. There is a potential scope for further establishing the claimed and observed beneficial effects in decreasing blood urea level.

**CONCLUSION:** There has been an increase in demand for phytopharmaceuticals all over the world because of the fact that allopathic drugs have more side effects. This forms a good basis for the selection of plants for further phytochemical and pharmacological investigation.

The Pharma-cological and clinical studies reported in the present review confirm the therapeutic value of *Tinospora cordifolia*. The presence of chemical compounds indicates that the plant could serve as “lead” for the development of novel agents for disorders in the coming years.

In this regard, further studies need to be carried out to explore *Tinospora cordifolia* for its potential in preventing and treating diseases. So, the present review gives a direction for future investigators to carry out research on the plant so that they could get some medicinally important drugs.

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