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Exploring the Anticancer Efficacy of Tinospora Cordifolia: Revolutionizing Cancer Care Through Herbal Science

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Abstract: Cancer continues to be one of the most impactful causes of morbidity & motility changes at the global level and it marked by the uncontrolled cell division of anomalous cell, however common treatment, like chemotherapy and radiation therapy, have a played important role, they have an effect beside of unwanted side effect, which allows researching an alternative therapies, a famous and traditional medicinal herb in Ayurveda medicine, tinospora cordifoila, it has acquired importance in the field of cancer treatment as it include various bio-active molecule such as alkaloids, glycosides, and diterpenoid lactones. In this review, we summarize the regulatory or modulating roles of Tinospora cordifolia on major molecular pathways, including NF-κB, apoptosis, angiogenesis inhibition, and help immune response have anticancer potential. In vitro & some limited clinical studies show efficacy against Breast, cervical, and brain cancer with very list side effects. But more large-scale clinical studies are needed to confirm its safety and efficacy in the human population.

Keywords: *Tinospora Cordifolia, Anticancer, Method of Preparation, Immune Modulation, Ayurvedic Medicine, Breast Cancer, Lung Cancer, Brain Cancer.*

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I. INTRODUCTION

Cancer is a major disease of cell proliferation characterized by progressive, persistent, abnormal, purposeless, and uncontrolled proliferation of tissue, which causes morbidity and mortality. Cancer cell produces Oncoprotein in the absence of growth factors or external stimuli. It also facilitate by oxidation and inflammation some time it induced by environmental factors which is causes DNA replication error According to the World Health Organization (WHO) global estimate report over 19.3 Mellon's new cases of cancer and 10 Mellon's death ratio in 2024 a India's cancer incidence is estimated at 1.15 million new patients in 2018and that ratio was increases in day by day, with older population and increasing exposure to risk factor like uses of tobacco, poor diets and also lack of physical activity. Therefore, according to that exposure, the global cancer incidence is expected to rise to 28.4 million cases in 2040. The majority of Cancer cases are found in the lung, breast, colorectal, and prostate cancer, and in a minor ratio of blood cancer. While modern science has the medicine to enhance survival rate, Doctors have treatment options such as chemotherapy and radiation therapies, which are associated with severe side effects such as tiredness, nausea, vomiting, hair loss, Anemia, bruising and bleeding, sore mouth, loss of appetite, skin and nail changes, and also sleep problems. There was a lot of ADR effect, which is why it needs the exploration of alternative and complementary therapies like herbal drugs such as tinospora cordifolia, which has a negligible amount of ADR effect and side effects.

A Tinospora cordifolia is the biological name of a topical plant which is known as giloye, guduchi, ammrutbhali, etc. Tinospora cordifolia is obtained in tropical regions of India, like Sri Lanka, which has garnered attention for its phytochemical properties, such as alkaloids, diterpenoids, and glycosides, supported by many studies.

It holds 2400 Ayurveda formulations as an ingredient. This formulation comes in more than 24 dosages, such as kwatha (decoction), hima (cold infusion), swarasa(juice), kolka (paste), gutika (tablets and pills), and avaleha (semisolid medicated confection), etc. [2]. Medicinal plants have been used as a source of medicine with their own personal ways, which have been passed from one generation to another. Owing to their versatile applications, plant-derived substances have recently become of great interest [6]

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II. PREPARATION

Plant material and preparation of Chloroform and Hexane extracts The 50% aqueous ethanolic extract (TCE) was obtained from the Indian Institute of Integrative Medicine, Jammu, India. 5 g of dried T. cordifolia stem powder was dissolved in 100 ml of a 50:50 aqueous ethanol solution. After the mixture had been left to sit overnight, it was filtered off and the dried massaged by hand. The freeze-dried TCE was then weighed, re-dissolved in distilled water, and used as an injection liquid. Adding n-Hexane to this concentrated TCE, the two were shaken together and then separated using a separating funnel. This process was repeated three times. The resulting hexane extract was evaporated to dryness on a rotary evaporator (BuchiLabortechnik , Switzerland) and labeled as Hex-TCE. The remaining substance was subjected to chloroform and separated through a Buchner funnel. The same separation procedure was then repeated once with the addition of heptane. [1]

III. BIOACTIVE COMPOUNDS

It belongs to diverse kinds of classes such as Alkaloids, Glycosides, Steroids, Diterpenoid lactones, Phenolics, Aliphatic, and other compounds [5]

A. Active Phytochemicals:

Tinospora cordifolia holds a bioactive compound such as be,

- *Berberine (Alkaloid) Contains 15 to 20 % of the Total Extract*
- *Berberine Chemical Structure No.1*

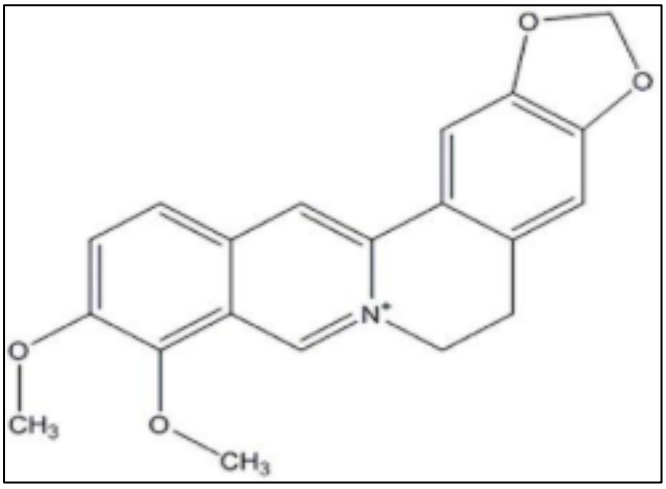

Fig 1 Berberine Chemical Structure No.1

- *Cordifoliaside (Glycoside) Contains 8 to 12% of the Total Extract*
- *Cordifoliaside Chemical Structure No.2*

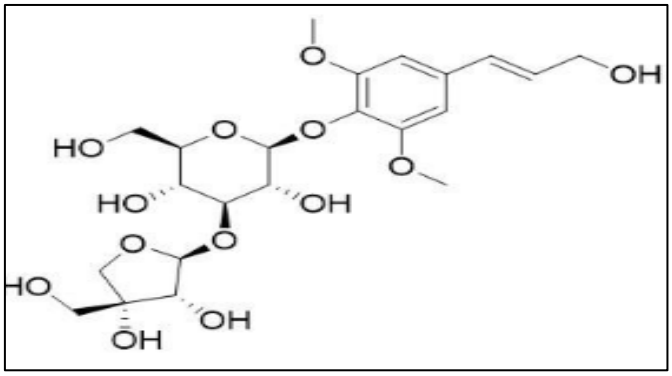

Fig 2 Cordifoliaside Chemical Structure No.2

- *Palmatine (Alkaloid) Contains 5 to 8% of the Total Extract*
- *Palmatine Chemical Structure No.3*

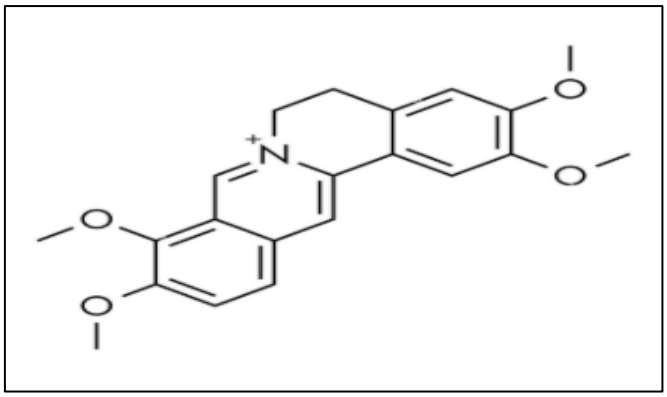

Fig 3 Palmatine Chemical Structure No.3

- *Magnoflorine (Alkaloid) Contains 3 to 5% of the Total Extract*
- *Magnoflorine Chemical Structure No.4*

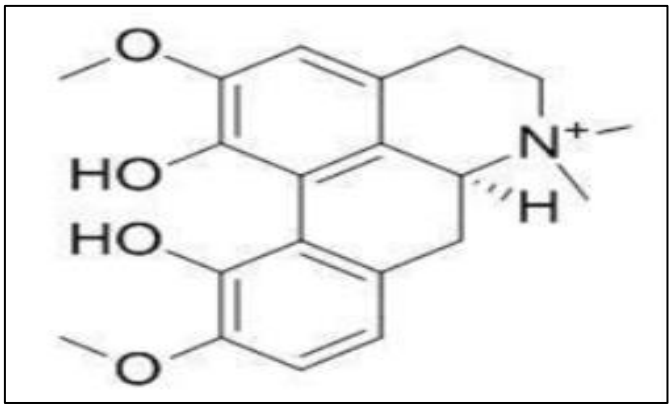

Fig 4 Magnoflorine Chemical Structure No.4

But berberine is considered the most active compound among these, and those handles showing anti-cancer, anti-inflammatory properties.

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Table 1 Constitution of Cordifolia (Guduchi) [4]

Type of chemical	Active principles	Part in which Present
Alkaloids (Tikta-Bitter principle	Berberine, Palmatine,	Stem
	Tembetarine, Magnoflorine, Choline, Tinosporin, Isocolumbin, Palmatine, Tetrahydropalmatine, Magnoflorine	Root
Glycosides	18-norclerodane glucoside, Furanoid diterpene glucoside, Tinocordiside, Tinocordifolioside,Cordioside, Cordifolioside A, Cordifolioside B,Syringin, Syringin-apiosylglycoside,Palmatosides C, Palmatosides F,Cordifoliside A , Cordiofoliside B,Cordifoliside C, Cordifoliside D, Cordifoliside E	Stem
Diterpenoid lactones	Furanolactone,Clerodane derivatives and[(5R,10R)-4R-8R-dihydroxy-2S-3R:15,16-diepoxy-cleroda-13 (16), 14-dieno-17,12S:18,1S-dilactone] and Tinosporon,Tinosporides and Jateorine, Columbin	Whole plant
Steroids	β -sitosterol, δ-sitosterol, 20 β-Hydroxy ecdysone.	Aerial part
	Ecdysterone, Makisterone A,Giloinsterol	Stem
Sesquiterpenoid	Tinocordifolin	Stem
Aliphatic compound	Octacosanol, Heptacosanol, Nonacosan-15-one 3,(α,4-di hydroxy-3-methoxy-benzyl)-4-(4-3, (α,4-di hydroxy-3-methoxy-benzyl)-4-(4-Compounds hydroxy-3-methoxy-benzyl)-tetrahydrofuran.	Whole plant
Miscellaneous	Jatrorrhizine. Tinosporidine, Cordifol, Cordifelone, N-trans-feruloyl tyramine as diacetate, Giloin, Giloinin, Tinosporio acid.	Root Whole plant

IV. MECHANISM OF ACTION

➢ *Understanding the NF-κB Pathway:*

The NF-κB (nuclear factor kappa B) signaling pathway is a critical regulator of immune response, inflammation, and cellular survival. It is NF-κB is activated by inflammatory signals such as TNF-α and IL-1, as well as microbial pathogens or tissue injury." In cancer, this pathway becomes deregulated, promoting tumor growth, angiogenesis, immune evasion, and resistance to apoptosis by upregulating genes such as BCL-2(B-cell lymphoma 2), BCL-XL (B-cell lymphoma extra-large), CYCLIN D1 (cell cycle regulator), and VEGF (vascular endothelial growth factor).

➢ *Pharmacokinetic Properties of Berberine:*

- Absorption: it has better absorption from tissues and muscles as well as oral absorption, but its oral bioavailability is too much less approx. 0.5 to 1.5%, and the Cmax level reached in 5-6 hours.
- Studies demonstrate berberine's benefits, and scientists are actively exploring innovative methods to improve its bioavailability.
- Distribution: it has having high volume of distribution (VD) in the tissue, especially the hepatic and kidney region. Berberine plasma protein binding is 85%.
- Metabolism: it is metabolized by microsomal enzymes like CYP2D6, CYP3A4. After metabolism, the obtained metabolite is demethylated Berberine.
- Elimination: Mostly it is excreted through bile and through urine, eliminating 8 -10%. There half-life (T½) is 4 to 5 hours.

- Prevent NF-κB Activation: - Barbering prevents the activation of NF-KB by suppressing IKK activation. This protein handles the activation of NF-KB. "NF-κB is inactive because it is held in the cytoplasm by the protein IKB. „ Activation of the NF-κB is an essential signal, like bacterial infection, inflammation, and stress signaling. To come IKK for degradation or phosphorylation of IKBα, after phosphorylation of IKBα, NF-κB is released, and it translocated to the nucleus.
- Reduction of Pro-inflammatory cytokines: - NF-κB plays a role in pro-inflammatory immune responses, growth regulation, such as TNF-α, IL-6, IL-1β, etc. It is connected to long-term inflammation near the tumor area. Tinospora cordifolia suppresses these immune factors, reducing their inflammatory environment that promotes tumor growth and spreading.

➢ *Suppression of Pro-Survival and Angiogenic Factors*

- Anti-apoptotic Genes: - Tinospora cordifolia can cure cancer in two ways.
- Enhance cancer cell death: - Tinospora cordifolia regulates the downstream anti-apoptotic gene factor as resulting in.

✓ BCL-2: - Protects cancer cells from dying. Keeps the cell alive and growing.
✓ BCL-XL: - It is like BCL-2, which also prevents cell death and supports cancer cell survival.
✓ CYCLIN D1: It handles cell growth and mitosis; it contributes to the formation of tumors.

- Starves tumor by blocking VEGF (anti-angiogenesis): - NF-κB translocation to nucleus modulates VEGF (angiogenic factor). This helps tumor growth by promoting blood vessels & nutritive material. Tinospora cordifolia inhibits VGEF production as well as NF-KB translocation, resulting in a lack of nutritive material and oxygen. The

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cell proliferation and suppression of angiogenesis speed will decrease.

➢ *Triggering Apoptosis*

Inhibition of NF-κB leads to promotion of apoptosis by Tinospora cordifolia via high-level expression of pro-apoptotic factors like Bax and caspases. These are decreased expressions of anti-apoptotic proteins like Bcl-2, Bcl-xl, and cyclin D1.

➢ *Antioxidant and Immune-8 Modulating Activities*

Not only this, but also many other well-known antioxidants Tinospora cordifolia, are also effective in scavenging reactive oxygen species (ROS), which are increased in cancer, and help the activation of NF-κB. Because it has a macrophage activity which is done by stimulates immune function, it also keeps of TH1/TH2 cytokine balance, which is involved in anti-tumor immunity.

➢ *Constructive Collaboration with Potential Other Therapies*

The inhibition of NF-κB by Tinospora cordifolia suggests efficacy to enhance the effect of traditional therapy, which is vulnerable to resistance mechanisms, for example up upregulating the activity of NF-κB after chemotherapy or radiotherapy. For greater comprehension of this, kindly refer to this [3]. The class of NF-κB proteins includes three that have a transactivation domain (RelA [p65], cRel, and RelB) and two that don't (p105/p50, p100/p52). Onlyp105/p50 and p100/p52 possess ankyrin repeats that serve as inhibitors to p52 and p50. However, all of them have a common Rel-homology domain, which handles such tasks as binding to DNA, dimerization, nuclear localization within cells, IKB binding, and exposure of its signal for nuclear import. The latter are requisite steps before the dimer can be translocated into the cell nuclei.[8]

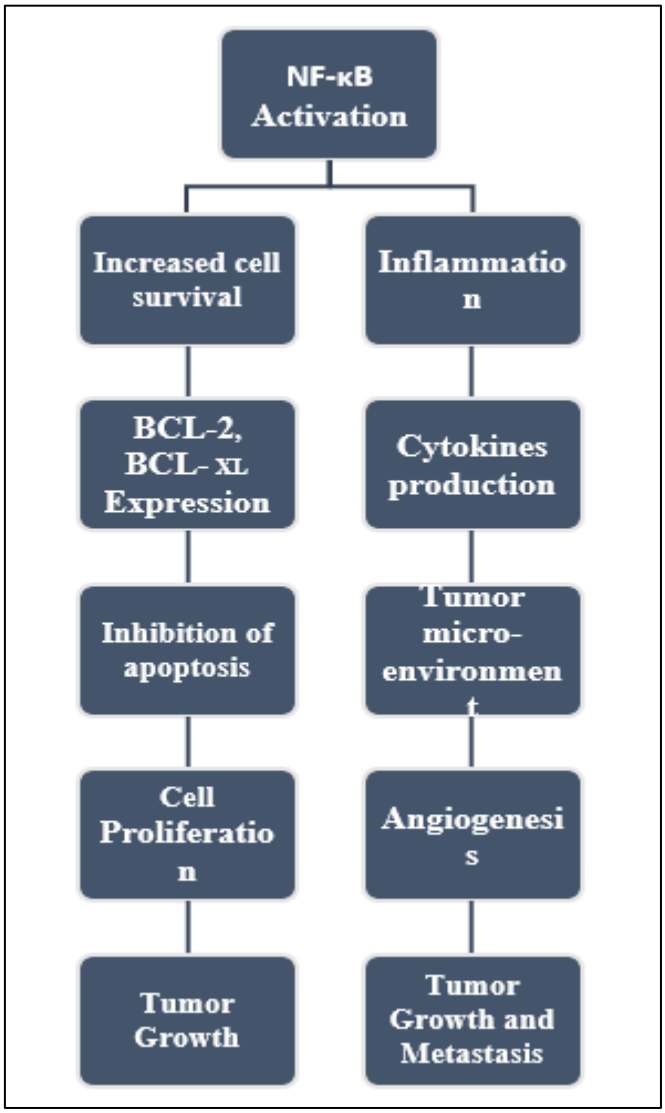

Fig 5 Growth of Cancer Cells by the NF-κB Pathway

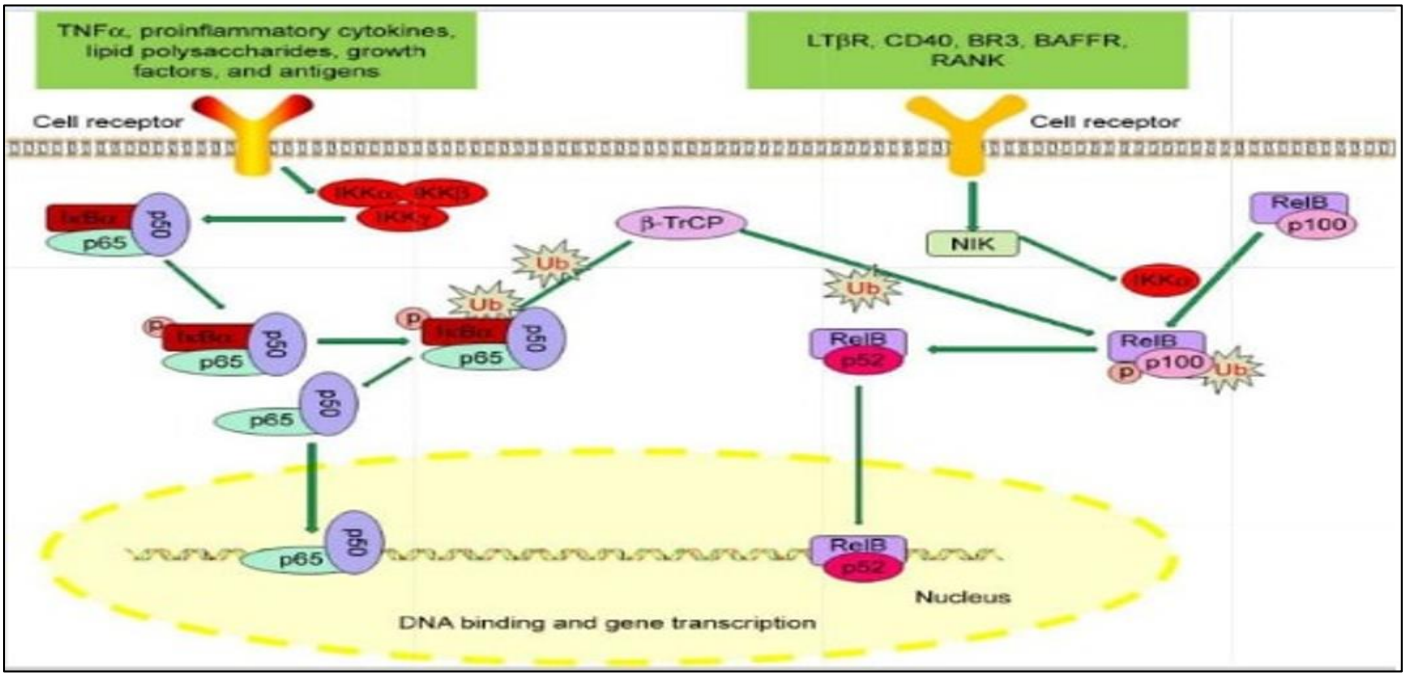

Fig 6 Molecular Pathways Governing NF-κB Transcription Activation

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V. MODE OF ACTION

➢ *The Anticancer Effects of Tinospora Cordifolia are Mediated Through Several Mechanisms of Action by Various Kinds of Gene Pathways:*

- Induction of Apoptosis: -Compounds in the plant trigger apoptosis in cancer cells via both intrinsic and extrinsic pathways. Key genes affected include BAX (pro-apoptotic) and BCL-2 (anti-apoptotic)
- Inhibition of Cell Proliferation: -Extracts inhibit cell cycle progression, effectively reducing cancer cell growth. Genes such as p53 (tumor suppressor) and cyclin D1 (cell cycle regulator) are involved.
- Anti-angiogenesis: -The plant's components prevent the formation of new blood vessels essential for tumor growth and metastasis. Genes like VEGF (vascular endothelial growth factor) are downregulated.
- Immune Modulation: - Tinospora cordifolia can help the immune system to elicit apoptosis of malignant cells. It regulates of NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) and Nrf2 (nuclear factor erythroid 2 related factor 2) pathway.

VI. IN VITRO STUDIES

➢ *Numerous in Vitro Studies have Examined the Effects of Tinospora Cordifolia Extracts on Different Cancer Cell Lines:*

- Breast Cancer: - The alcoholic extract of tinospora cordifolia shows the cytotoxic and dose-related response inhibitory effect on human breast cancer cell MDA-MB231. The 50% concentration methanolic extract T.C used against MDA-MB231 was found to be 59mg/ml in 0.25% dimethyl sulfoxide (DMSO) and 50 mg/ml in 0.5% dimethyl sulfoxide (DMSO).[7]
- Anti-proliferative activity: -In the lab tests, TCE measures the proliferating activity against the (HELA) cervical cancer cell by MTT Assay: The MTT assay is a helpful method to find the cell proliferation and cytotoxic. This study examined the toxic impact of tinospora cordifolia extract fragments on HELA cells by measuring the reduction of yellow tetrazolium dye 3- [4,5-dimethylthiazol-2-yl]-2,5-diphenyl MTT to formazan crystal. [9]
- Lung cancer: - AgNPs affected human lung carcinoma cell (A549) viability percentage: In an in vitro study, it saw AgNPs having AgNP's cytotoxic activity, which was assessed against human lung cancer cell A549. A dose-dependent reduction in the relative cell viability percentage of A549 cells after incubation with AgNPs for 24 h was seen from the result of MTT assays. At higher concentration, Considerable cell mortality was observed [10]
- Brain cancer: - U87MG glioblastoma and IMR-32 neuroblastoma cells were seeded in 24-well plates at a seeding density of 10,000 cells/ mL and treated with Chl-TCE (10 mg/mL) and Hex-TCE (15 mg/mL). Primary astrocytes and hippocampal neurons were seeded at 20,000 cells/mL plating density, followed by the same treatment regimen.[1]

VII. CLINICAL STUDIES

A clinical trial was done in Dravya Guna postgraduate department of the Uttaranchal Ayurveda College in Dehradun, Uttarakhand, which affirmed its legality. There was conducted phase-1 clinical trial was conducted where 56 volunteers were selected. Among the 38 patients were those under contract from the Goudham Cancer Treatment and Research Center in New Delhi.[11]

- The drug origin and Authenticity: - the clinical investigation of Tinospora cordifolia (giloye) stems come from a Dehradun market. Chopped Tinospora cordifolia stem fragments were used to make its dosage form.
- Medicine Preparation for Clinical Trials: A 5 kg bioactive stem is collected, and it is transferred to a reputed pharmaceutical company to make dosage forms like tablets, capsules, etc. A tablet is made for clinical trial and proper handling and administration, which is known as Gilo Vati.
- Suggested Dosage: Take 2 tablets with lukewarm water after a meal (TID) three times a day.
- Patient counting and selection: A total of 56 volunteers were selected for the clinical trials, and only 38 patients completed the clinical trials; the remaining 18 patients who did not show any improvement were then enrolled at Uttaranchal Ayurvedic Hospital, found on Rajpur Road in Dehradun. 38 of the patients were contracted from the Goudham Cancer Treatment and Research Center in New Delhi.

- *They are Divided into II Groups, Group A and Group B*

✓ Group A: - there is no experimental sample given (chemotherapy is ingested)
✓ Group B: - In group B, patients are given T. Cordifolia
✓ Intervention Duration: - Approx. Three months.
✓ Follow up: - To figure out whether adjuvant therapy was beneficial in reducing the adverse drug effect of chemotherapy for the whole 3 months. Three-month follow-up was conducted after the clinical study.
✓ Started: - The first month, and the next follow-up after 2 months and followed by the final follow-up 1 month.

- *Patient Selection:*

✓ Inclusion: - A cancer patient who was shown or diagnosed at stage 1 or stage 2, going through chemotherapy. Their age criteria are 20 to 60 who have short-term severe adverse effects from chemotherapy.
✓ Excluding: - Rather than stage 3 and stage 4 patients, these are patients who had already had long-term local adverse effects. This patient has several infections, which cause grave consequences and complicated health issues such as mental disorientation, hepatic problems & chronic renal failure. This patient's age is like that of patients 20 to 60.

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VIII. CONCLUSION

One such natural product that holds tethering potential as an adjunctive therapy in cancer treatment is an Ayurveda herb called Tinospora cordifolia. Due to its bioactive compounds, it shows potent anticancer capabilities via apoptosis, inhibiting angiogenesis, suppressing tumor growth, and improving immune modulation. The targeting of many pathways, such as NF-κB, that are crucial during the carcinogenesis process, proves its potential as an adjunct in diminishing side effects and enhancing the therapeutic activity of traditional agents like chemotherapy and radiotherapy. However, despite promising in vitro and sparse clinical results, extensive large cohort clinical trials are needed to accept its safety, efficacy, and applications in integrative oncology. As promising as Tinospora cordifolia is, with the potential for radically transforming successful cancer treatment, there is an absolute need for further investigations and formal formulation of these products.

REFERENCES

[1]. Sharma, A., Saggu, S. K., Mishra, R., & Kaur, G. (2019). Anti-brain cancer activity of chloroform and hexane extracts of Tinospora cordifolia Miers: an in vitro perspective. *Annals of Neurosciences*, *26*(1), 10–20. https://doi.org/10.5214/ans.0972.7531.260104

[2]. Bhatt, M. L. B., Ministry of Ayush, Government of India, Ministry of Ayush, GOI, India, DG (I/c), CCRAS, New Delhi, Director, Ramaiah Indic Specialty Ayurveda, Bengaluru, Head, Dept. of Neurology, K.G. Medical University, Lucknow, Senior Principal Scientist, CSIR-Institute of Genomics & Integrative Biology, New Delhi, & Associate Professor, All India Institute of Ayurveda, New Delhi. (2022). Guduchi (Tinospora cordifolia) Technical Dossier. https://www.researchgate.net/publication/366953016_Technical_Dossier_on_Guduchi_Tinospora_cordifolia

[3]. Lin, Y., Bai, L., Chen, W., & Xu, S. (2009). The NF-κB activation pathways, emerging molecular targets for cancer prevention and therapy. *Expert Opinion on Therapeutic Targets*, *14*(1), 45–55. https://doi.org/10.1517/14728220903431069

[4]. Upadhyay, A., Kumar, K., Kumar, A., & Mishra, H. (2010). Tinospora cordifolia (Willd.) Hook. f. and Thoms. "(Guduchi) - Validation of the Ayurvedic pharmacology through experimental and clinical studies." ("Tinospora cordifolia (Willd.) Hook. f. and Thoms. (Guduchi ...") International Journal of Ayurveda Research, 1(2), 112. https://doi.org/10.4103/0974-7788.64405

[5]. Shah, M. S., 1, Shinde, A. R., 2, Jagtap, D. R., 3, Kamble, S. M., 4, Nagargoje, S., 5, Shewale, K. P., 6, & Oswal, R. J., 7. (2020). "TINOSPORA CORDIFOLIA: ONE OF THE AYURVEDIC PLANTS OF CORONIL FORMULATION FOR COVID-19." ("Tinospora cordifolia (Willd.) Hook.f. & Thomson: A Review of its role ...") In European Journal of Biomedical and Pharmaceutical Sciences (Vol. 7, Issue 8, pp. 257–267). http://www.ejbps.com

[6]. "Polu, P. R., Nayanbhirama, U., Khan, S., & Maheswari, R. (2017)." ("Bio-efficacy and Radical scavenging activity of Terminalia paniculata") "Assessment of free radical scavenging and anti-proliferative activities of Tinospora cordifolia Miers (Willd)." ("Characterization of phytochemicals and validation of antioxidant and ...") BMC Complementary and Alternative Medicine, 17(1). https://doi.org/10.1186/s12906-017-1953-3

[7]. Ahmad, R., Srivastava, A. N., & Khan, M. A. (2015). Evaluation of in vitro anticancer activity of the stem of Tinospora cordifolia against human breast cancer and Vero cell lines. Journal of Medicinal Plants Studies, 3(4), 33–37.

[8]. Role of the NFκB-signaling pathway in cancer. (2018). In OncoTargets and Therapy (Vol. 11, pp. 2063–2073). http://dx.doi.org/10.2147/OTT.S161109

[9]. "Polu, P. R., Nayanbhirama, U., Khan, S., & Maheswari, R. (2017)." ("Bio-efficacy and Radical scavenging activity of Terminalia paniculata") "Assessment of free radical scavenging and anti-proliferative activities of Tinospora cordifolia Miers (Willd)." ("Characterization of phytochemicals and validation of antioxidant and ...") BMC Complementary and Alternative Medicine, 17(1). https://doi.org/10.1186/s12906-017-1953-3

[10]. Mittal, J., Pal, U., Sharma, L., Verma, A. K., Ghosh, M., & Sharma, M. M. (2020). ("Plant-mediated synthesis of silver nanoparticles: unlocking their ...") Unveiling the cytotoxicity of photosynthesized silver nanoparticles using Tinospora cordifolia leaves against human lung adenocarcinoma A549 cell line. ("Teaching Faculties") *IET Nano biotechnology*, *14*(3), 230–238. https://doi.org/10.1049/iet-nbt.2019.0335

[11]. Pawar, A. R., Chougule, A. T., Kamble, J. R., Salokhe, P., Chougule, N. B., & Ashokrao Mane Institute of Pharmacy. (2024). Tinospora cordifolia – as an anticancer agent: recent and advanced study. In *INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES* (Vol. 2, Issue 1, pp. 707–716) [Journal-article]. https://doi.org/10.5281/zenodo.10578070