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Review on *Trichosanthes species*:Deserving Potential Pharmacological Properties and Boon in Medical Applications

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ABSTRACT

Trichosanthes species of the *Cucurbitaceae* family, fruits of this species are good potential sources of various phenolic compounds and antioxidants with anticancer, antiproliferative, cardioprotective and antioxidant properties. Many research studies on *Trichosanthes species* reported that it contains important protein constituent known as Ribosome Inactivating Protein (RIP), it helps in formulation of anticancer agents. Biological components in species are valued as a stimulant for it medical properties like Anti-inflammatory, Antidiabetic, Antiulcer and Cardioprotective activities. This review is focused on emphasizing varied pharmacological properties of *Trichosanthes species* and its future prospects for improved usage in treating numerous conditions.

Keywords- *Trichosanthes species,* Pharmacological properties, Anti-HIV, Anticancer and Apoptosis.

INTRODUCTION

Among all biological life forms plants play a crucial role in the environment by supporting all types of biological life forms. They also play a promising role in the treatment of diseases established by their employment in all important systems of medicine. One such plant species is *Trichosanthes*.Most of these plants species are rich in flavonoids, carotenoids and phenolic compounds. These species play an important role in the Ayurvedic and Siddha system of medicine due to its various medicinal values like anti HIV[3], cardioprotective[33], anti-ulcer[34], anti-diabetic[35], hepatoprotective[37], anti-inflammatory[39], larvicidal effects[38] etc.

In the present review focuses on update on the plant species mainly on *Trichosanthes* has been enlightened to bring out the hidden medicinal values of thisspecies. The genus *Trichosanthes* is native to Southern and Eastern Asia, Australia and Islands of the western Pacific.

It was probably domesticated in ancient times in India. It is grown as vegetable in many countries of tropical Asia and Africa. It is also reported from India through Malayato tropical Australia *Trichosanthes species* is an introduced crop of increasing importance in several parts of Africa, including Ghana and Nigeria. The genus *Trichosanthes* comprises about 100 species, of which a few have been domesticated in Asia. They are the wide variation of *Trichosanthes* species occurring from India, Srilanka, China, through South-East Asia, northern Australia, tropical regions of Bangladesh, India, Nepal, Pakistan Srilanka, Myanmar, Vietnam, Indonesia, and Malaysia, Philippines, in Australia it is found in Northern Territory, Queensland and in Western Australia[1].

Bacterial resistance is a worldwide emerging problem. During the last ten years the pace of development of new antibacterial drugs has slowed down, while the prevalence of resistance (especially multiple) has increased astronomically. The effects of plant extracts on bacteria have been studied by a very large number of researchers in different parts of the world. Much work has been carried out on ethno medicinal plants in India and other parts of the world very interestingly, Outcomes of this research are very beneficial to the human race to clear the problems of the different diseases. It has been suggested that the aqueous and ethanol extracts from plant susedinallopathicthe antidiabetic, hepato-protective and antioxidant potential of *Trichosanthes species*. The present review explores the potential activity of *Trichosanthes species* against viral, bacterial, fungal diseases[1].

Cucurbitaceae family

The family *Cucurbitaceae* (vine crops) contains of various squashes, melons, and gourds, including crops like cucumber, pumpkins and watermelons. The family of *Cucurbitaceae* lies within the class of dicotyledonous and in the division of anthophytha. It is known to many as the gourd or pumpkin family. They usually produce spiraling tendrils or modified shoots that wrap around adjacent objects and use them for their support. Cucurbits generally are climbing plants with alternate, simple, palmately veined leaves and dioecious species. Many chemical studies reveal that in addition to a number of tetra and pentacyclic triterpenes, the toxic bitter principles cucurbitaceous (a group of often highly oxygenated tetra cyclic compounds with a unique carbon skeleton and almost a carbonyl group in ring C) may be considered as a taxonomic character of Cucurbitaceae[1].

Trichosanthes cucumerina

It is a tropical or subtropical vine, raised for its strikingly long fruit as well. It is used as a vegetable, medicine and a lesser known use in crafting didgeridoos. Common names include snake gourd (var. *anguina*), serpent gourd, chichinga, and padwal. It is also known as chichi do in Nepali Formerly, the cultivated form was considered a distinct species, but nowadays it is regarding as mere variety of the wild ancestor, as they freely interbreed *Trichosanthes cucumerina* var. *anguina* (L.). Haines–cultivated variant with *Trichosanthes cucumerina* var. *Cucumerina*-wild variant. It is rich in various essential proteins and vitamin C. The major active constituents of the drug are triterpenoid, saponins, and cucurbitacins; chemical constituents like Flavonoids, carotenoids, phenolic acids which makes the plant pharmacologically as well therapeutically active. Trichosanthes cucumerina is used in the treatment of headache, alopecia, fever, abdominal tumors, bilious, boils, acute colic, diarrhea, hematuria and skin allergy etc.

Trichosanthes cucumerina is used as an abortifacient, vermifuge, refrigerant, purgative, malaria, laxative, hem

agglutinant, emetic, cathartic, bronchitis and anthelmintic. A novel is flavone glucosidal, 5, 6, 6'-trimethoxy-3', 4'-methylene-dioxyisoflavone- 7-O-beta-D- (2"-O-p-coumaroylgluco -pyranoside)[1] has been characterized from the seeds of Trichosanthes. The positive effects of the plant are due to the presenceantioxidants in it. The dried seeds in are used for various ailments because of anthelmintic and antidiarrheal properties in it. Seeds have anti-bacterial, anti-spasmodic and insecticidal properties. Hot aqueous extract (HAE) of root tubers of Trichosanthes cucumerina exhibited significant anti-inflammatory activity.

The root extract of *Trichosanthes cucumerina L*. and the fruit juice tested cytotoxicity against human breast cancer cell lines, lung cancer cell lines and one colon cancer cell line with positive effect. The root extract inhibited more strongly than the fruit juice. Crude Ethanolic extract (EE) of *Trichosanthes cucumerina* showed significant blood glucose lowering activity in alloxan diabetic albino rats. The acetone extract of leaves of *Trichosanthes cucumerina* showed moderate larvicidal effects. Hot water extract (HWE) of aerial parts of *Trichosanthes cucumerina*noted to improve glucose tolerance and tissue glycogen in non-insulin dependent diabetes mellitus induced rats. Recent studies have showed that the drug possess antidiabetic activity with volume improvement in oral glucose tolerance and glucose uptake in peripheral tissues[1].

Trichosanthes dioica

It is widely cultivated in the eastern part of the India from longtime. It is employs as an ingredient of soup, stew, curry, sweet, or eaten fried. It is a good source of carbohydrates, tannins, saponins, vitamin A and C. It also contains trace elements (such as magnesium, potassium, copper, sulphur, and chlorine) which were needed in small quantities. Pointed gourd is rich in vitamins and minerals.

The seeds of *Trichosanthes dioica* contain a large amount of peptides. These peptides have the unique property of being resistant to the action of silver nitrate, a sensitive reagent commonly used to stain proteins. The seed extract of *Trichosanthes dioica* consists of oxidihydrokarounidol-3-benzoate as the most predominant component in the highly polar fraction of the non saponifiable lipid. Two main phytosterols in *Trichosanthes dioica* are namely, 24α- ethylcholest-7-enol and 24β-ethylcholest-7-enol. Seeds of *Trichosanthes dioica* also contain lectin, a carbohydrate (specifically galactose) binding protein which is homologous to Type-II ribosome inhibitory proteins (Type-II RIP)[1].

Trichosanthes kirilowii

It is a flowering plant from the Cucurbitaceae family found particularly in Henan, Shandong, Hebei, Shanxi, and Shaanxi. It is one of the 50 fundamental herbs used in traditional Chinese medicine, where it shares the name *gualou*with the related *Trichosanthes rosthornii*. The plant is a good source of the toxic anti-HIV type I ribosome-inactivinglectin Trichosanthin several multi-florane triterpenoid has been isolated from the seed extract. The most predominant ones include karounidiol and its 3-O-benzoate derivative. These triterpenoid are expected to be potential anti-tumor promoters[1].

Trichosanthes tricuspidata

It known as *T. palmate Roxb, T. bracteata Lamb, T. puberaBlume or Modecccabracteata*belongs to the family of Cucurbitaceae. The fruits consists cucurbitane, hexanorcucurbitane and octanorcucurbitane glycosides. From the fruits of *T. tricuspidata*, 14 cucurbitane glycosides were isolated namely cucurbitacins K, 2-O-β-glucopyranoside, a

hexanor cucurbitaneglucosidal and octanorcucurbitane glucosidal were isolated along with two known cucurbitane glucosidal. An extract of the fruits of this plant was found to be cytotoxic in KB cells, two new cucurbitacins were reported: tricuspid tin and 2-O-glucocucurbitacin.

The root of plant contains methyl palmitate, palmitic acid, suberic acid, α-spinasterol, stigmast-7-en-3-beta-ol, α-spinasterol 3-o-beta-D-glucopyrano side, stigmast-7-en-3-beta-ol-3-O-beta-D-glucopyranoside, glyceryl 1-palmitate, glyceryl 1-stearate, bryonolic acid, cucurbitacins B, isocucurbitacin B, 3-epi-isocucurbitacin B, 23, 24-dihydro-cucurbitacin D, isocucurbitacin D and D-glucose as well. And three new cycloartane glycosides have been isolated and named cyclotricuspidosides A, B and C from the leaf and stem parts[1].

Trichosanthis radix

This is a flowering plant in the family *Cucurbitaceae*. *Trichosanthis radix* extract has function to relieve pyreticosis, polydipsia, swelling on the body surfaceand ulcer as well.Extract can be used in food, beverage, health supplement and medicine. Although *Trichosanthes species* have been using from ancient times but the discovery of significant activities of *Trichosanthes species* started a new era in drug development mainly against the carcinogenic diseases. This biological component is easily available in nature, amenable to animals and hostile to wide range of diseases.

The main aim of this review is to investigate the past and current strategic developments in the use of *Trichosanthen species* against wide range of diseases and conditions. It also emphasizes on more potential use of this plant species for advanced drug developments.

PHARMACOLOGICAL PROPERTIES

Trichosanthen (TCS) is polypeptide composed of a single polypeptide chain with a molecular weight of 27 kDa. Its amino acid sequence demonstrates homology to the A chains of many type II RIPs, such as ricin A chain. It inhibits protein synthesis by cleavage of the N–C glycosidic bond of adenine 4324, the 4324th base of 28S rRNA. This action renders the ribosome incapable of binding elongation factor 2 and finally terminates translation.TCS owns a wide spectrum of biological and pharmacological activities. It can produce adverse effects on reproduction in the mouse by causing follicular atresia and degeneration of ovulated oocytes[2]. In fertilized animals, TCS elicits death of syncytiotropho-blasts of placental villi, and its results, the embryo fails to develop. This action is related to its uptake by placental trophoblast cells. TCS exhibits various activities such as immunomodulatory (immunosuppressive), anti-tumor, anti-viral, and anti-human immunodeficiency virus (HIV) activities. Its anti-HIV activity is attributed to inhibition of the replication of HIV and cytotoxicity to HIV-infected cells mainly macrophages and lymphocytes. The fact that TCS was applied in the treatment of choriocarcinoma is consistent with its abortive activity, since this tumor also originates from fetal trophoblast cells.

Effect of Trichosanthin (TCS) on HIV

Li *et al*., in the year 1991 demonstrated that TCS has anti-HIV activity.TCS is a type I ribosome-inactivating protein (RIP) with potent inhibitory activity against human immunodeficiency virus(HIV) type 1, and has been clinically applied in acquired immunodeficiency syndrome (AIDS) therapy. HIV is a lent virus (slowly replicating retrovirus) that causes the Acquired Immuno Deficiency Syndrome

(AIDS). HIV infects vital cells in the human immune system such as helper T cells (specifically $CD4^+$ Tcells) and macrophages. Since the beginning of the epidemic, almost 75 million people have been infected with the HIV virus and about 36 million people have died of HIV recently. Globally, 35.3 million [32.2–38.8 million] people were living with HIV at the end of 2012(retrieved from W.H.O).

In the late 1980s, the anti-viral effects of TCS against HIV-1 were described Phase I and II clinical trials were conducted in the USA to evaluate the safety and potential efficacy of this drug. It was shown that TCS elicits a moderate increase in circulating CD4þ T cells and a significant decrease of virus load in acquired immunodeficiency syndrome (AIDS) by the time patients had failed treatment withazido thymidine(i.e.TCS is more effective than antiretroviral agents such as azidothymidine; usedagainst AIDSvirus). In addition to TCS, many other RIPs including Momordica anti-HIV protein, pokeweed anti-viral protein, and Gelonium anti-HIV protein (GAP31), have been reported that these can inhibit HIV-1 replication *invitro* successfully. It was initially thought that TCS inhibits HIV by halting protein translation through RIP activity but it inhibits the replication of HIV-1 *invitro* and decreases HIV markers, good progress has been observed with the elucidation of the anti-tumour and anti- HIV mechanism of TCS, including the observation that N- terminal sequences of TCS has anti-tumour activity and the anti-HIV property of TCS is due to inhibition of HIV-1 integrase. JAR cells (a human choriocarcinomaline) are sensitive to TCS and are useful model for cell biological study. Study the effects of TCS on JAR cells going to help us to understand better the anti-tumour and anti-HIV mechanism of TCS.

Li *et al* reported that even small amounts of TCS specifically inhibit HIV without obvious ribosome inhibiting effects, whereas large amounts induce apoptosis in HIV-1 infected cells. TCS inhibits HIV-1 integrase and cleaves supercoiled DNA *invitro*. It is also associated with and stimulates the activation of chemokine receptors. TCS is a membrane-permeate peptide that is believed to act within the cell and need cross the membrane barrier for its action. TCS interacts with and inserts into artificial phospholipids membrane. It induces membrane fusion of liposome. It was also reported that TCS hijacks the cell-derived exosomes for intercellular transport. Li *et al*studied the physical relationship between TCS and HIV-1, showed that TCS penetrated into viral particles. The penetration had no obvious effect on viral integrity and also identified important sites for the penetration and revealed that this penetration may be important for virus elimination. Therefore Li *et al* concluded that TCS having anti HIV activity results no side effects[3].

Effect on various Cancer cell lines

Cancer known medically as malignant neoplasia, is a broad group of diseases involving unregulated cell growth. In cancer, cells divide and grow uncontrollably, forming malignant tumors, which may invade nearby parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Cancer is a leading cause of death worldwide and accounted for 7.6 million deaths (13% of all deaths) in 2008. Cancer is usually treated with chemotherapy, radiation therapy and surgery in 2007, cancer caused about 13% of all human deaths worldwide (7.9 million).The era of chemotherapy for cancer began in the 1940s with the first use of nitrogen mustards and folic acid antagonist drugs. Namely carboplatin (Paraplatin), cisplatin (Platinol, Platinol-AQ), cyclophosphamide (Cytoxan, Neosar),

doxorubicin (Adriamycin), etoposide (VePesid), fluorouracil (5-FU). Major side effects of cancer drug includes Numbness or tingling in the fingers or toes, weakness , loss of reflexes, jaw pain, hair loss (reversible), decrease in blood cell counts, allergic reaction, nausea and vomiting, loss of appetite, change in taste.

Trichosanthin (TCS) is a promising agent for the treatment of cancer.Many of the reports showed that TCS inhibited cervical adenocarcinoma HeLa cell proliferation through the PKC/MAPK/CREB signal pathway. Furthermore, TCS down-regulated Bcl-2 expression, which was abrogated by a cyclic AMP-responsive element (CRE, TGACGTCA) decoy oligonucleotide (OGN), is blocking the CRE-binding protein (CREB) binding site on Bcl-2 successfully. These results suggest that CRE-mediated gene expression may play a pivotal role in HeLa cell proliferation. However, little is known about the effect of TCS on cell cycle arrest of HeLa cell, cervical squamous carcinoma (Caski and C33a cell), and human pancreatic carcinoma (SW1990 cell), especially, whether genes related to cell cycle are regulated by the CRE decoy OGN. The effects of TCS on the proliferation of cancer cells, cell cycle arrests in the progress of cell proliferation and the role of CRE in cell cycle regulation.

Bhattacharya*et al*in the year 2011, study evaluated Antiproliferative effect of hydroalcoholic extract from *Trichosanthes dioica* root (TDA) on Ehrlich as cites carcinoma (EAC) cells *invitro*. The cytotoxic activity of TDA against EAC cells was assessed *invitro* by assays trypan blue cell viability assay and MTT cell proliferation assay. Results of Bhattacharya*et al*study revealed that TDA at all test concentrations exhibited significant increment in non-viable cells in trypan blue cell viability assay as compared to vehicle control but the percentage of non-viable cells were found to be increased up to a concentration of 4µg/ml of TDA, followed by a decrease i.e., on further increasing the TDA concentration, the non-viable cells were found to be decreased there by demonstrating the maximum cytotoxic effect at the concentration of 4µg/ml. In case of MTT cell proliferation assay, the percent cytotoxicity increased up to a concentration of 2µg/ml of TDA, followed by a decrease i.e. further increase in TDA concentration lead to gradual decrease in cytotoxicity there by demonstrating the maximum Antiproliferative effect at the concentration of 2µg/ml. The hydro alcoholic extract of *T.dioica* root has significant Antiproliferative effect at lower concentrations against Ehrlich as cites carcinoma cells *in vitro*, thus suggesting the feasibility of its possible promise as natural anticancer agent[5].

Trichosanthin (TCS) has been reported to be effective against a variety of other tumors including hepatoma, colon carcinoma, stomach cancer, lung cancer, breast cancer, prostate cancer, and melanoma. Some early research reported that TCS did not exert much toxicity to hepatoma cell lines, including H35 and HepA-H. However, when epidermal growth factor (EGF) is conjugated to TCS, the immunotoxin EGF-TCS is toxic to hepatoma cells, for example BEL-7402, MCF-7, and BGC-823. In addition, EGF-Trichosanthin also has *invivo* anti-hepatoma effects when the hepatoma animal model is constructed by injection of BEL-7402 cells. Dexamethasone enhances the effects of Trichosanthin on apoptosis in HepG2 cells by inhibiting the NF-JB Signaling pathway, which highlights the possibility of combined drug application of Trichosanthin and dexamethasone in the clinical treatment of hepatoma[6].

Studies also disclose that Trichosanthin exhibits an anti-colon carcinoma effect in both *invitro* and *invivo*

experiments. When Trichosanthin gene is cloned and expressed in colorectal carcinoma Lo Vo cells and it evokes apoptosis in these cells. Not only colon carcinoma cell line CT-26, but also *in vivo* colon carcinoma produced by Sw-1116 cells, noticed that it is sensitive to Trichosanthin toxicity[7].

Trichosanthin plays a distinct role by producing toxic effects on MCG803 cells of the stomach adenocarcinoma, another cancer of the digestive system[8]. An animal model of lung cancer was created by administration of A549 cells to nude mice. In Li *et al.,* research they observed that Trichosanthin has the ability of either prevent or inhibit the process of lung tumor genesis[9]. In another *Invivo* experiment, Trichosanthin elicits an anti-tumor immune response in a murine Lewis lung cancer model by boosting the interaction between tumor suppressor in lung cancer 1(TSLC1) and class-I MHC-restricted T cell-associated molecule (CRTAM). TCS inhibits the proliferation of MDA-MB-231 and MCF-7 cells and the growth of transplanted breast cancer in nude mice. For prostatic cancer, Trichosanthin can induce apoptosis in RM-1 cells, and an induction of apoptosis is a very important mechanism of TCS to inhibit this type of cancer. TCS can also markedly inhibit melanoma cells by the suppression of DNA synthesis in S phase and cell mitosis as well as induction of cell apoptosis.

In the year 2007, Zhang*et al.,* demonstrated that TCS has activity against leukemia[10]. In 1990s, TCS was found to be toxic to leukemia/lymphoma cells *invitro*[11,12] experiments.A decade later, TCS was reported to exert an antitumor action on chronic myelogenous leukemia K562 cells and acute T cell leukemia Jurkat cells. TCS caused a down-regulation of p210Bcr-abl and its downstream signals, results in tyrosine kinase inhibition in K562 cells[10]. Both PKC inhibition and caspase 3 activation are involved in TCS-induced apoptosis in K562 cells[13]. Under similar conditions, TCS is more toxic to HUT78, MOLT-4, Jurkat, and CEM cells originating from T lymphocytes and macrophages than Raji and Daudi cells from B lymphoma[14].

Trichosanthin inhibits the tumor cell proliferation by various mechanisms i.e. TCS suppresses adenyl cyclase activity and thus reduces cyclic AMP (cAMP) levels in HeLa cells. It was noticed that decrease in protein kinase C (PKC) level rather than protein kinase A (PKA) level in these cells. This is different from the conventionally accepted mechanism. In another experiment,Wang *et al*in the year, 2010 reported that TCS inhibits cell proliferation in different tumor cells through different pathways and mechanisms, which merit further in-depth cell death pathway in HeLa cells[16]. And also stated PKA and PKC activities were significantly inhibited in TCS-treated HeLa cells and although a specific PKA inhibitor failed to affect the effects of TCS, and PKC activator/inhibitor significantly attenuated/enhanced the inhibitory effect of Trichosanthin on cell proliferation. The inhibition of PKC was found to be involved in the apoptotic pathway induced by TCS in K562 cells. The transcriptional factor cAMP response element binding (CREB) protein, a downstream molecule in cAMP/PKA pathway was found to participate in the TCS-induced cell death pathway in HeLa cellsactively. CREB phosphorylation was significantly decreased through cAMP inhibitor and but not by a PKA inhibitor. These mechanisms infer that HeLa cell proliferation was inhibited by TCS via suppression of the PKC/MAPK signaling pathway.

Trichosanthin induces a rapid decline in nuclear factor kappa B (NF-kB) and cyclooxygenase-2 (COX-2) expression leading to apoptosis in hepatoma HepG2 cells. The suppression of NF-kB and COX-2 protein has been suggested to be the most

important factorfor the antiproliferative and proapoptotic effects on cancer cells. COX-2 may lie downstream of NF-kB. Since the inhibition of NF-kB can ensue in down-regulation of COX-2. TCS also down-regulated p210 (Bcr-Abl), protein tyrosine kinase (PTK), and heat shock protein 90 (Hsp90) in chronic myelogenous leukemia K562 cells. All these genes and proteins are associated with proliferation of cancer cells, and their inhibitors have been studied to treat a variety of cancers in clinics. All these data suggested that HeLa cell proliferation was inhibited by TCS via suppression of the PKC/MAPK signaling pathway.

Trichosanthin effects cervical cancer by its unique activity. Cervical cancer is the one of the majorly affecting caner in human population. It was observed that when TCS was added to cultured tumor cells, it brought about a reduction in the uptake of radioactive precursors for protein synthesis. This suggested that TCS killed cells by virtue of its RIP activity. Many Scientists first tested the toxic effects of TCS on HeLa cervical cancer cells and it has manifested inhibitory effectssignificantly. It heightened cytosolic calcium and suppressed intracellular cAMP/protein kinase C (PKC) levels via PKC inhibition. Different from usual RIP activities, TCS brings about apoptotic cell death in HeLa cells, and activation of caspase 8, 9 and 3 has been observed[15]. The up regulation of ER chaperone immunoglobulin heavy chain-binding protein (BiP) and C/EBP homologous protein (CHOP) and activation of caspase 4 suggest the participation of the endoplasmic reticulum stresses pathway in TCS-induced HeLa cell apoptosis[17]. Recent studies have also demonstrated the toxicity of TCS on cervical cancer Caski cells and it plays a role in demethylation by inhibiting DNA (cytosine-5)-methyltransferase 1 (DNMT1) enzyme activity, DNM1 mRNA and protein expression in CaSki cells. The demethylation of TCS in HeLa cells takes place via attacking TSLCl and p16 genes. In the year 2009, Zhang Y*et al*. established an animal model of cervical cancer by repeated injections of mouse U14 cell line into Kunming mice. TCS potentiated the humoral immunity in mice by a minor dosage levels[18].

Ng*et al*., in the year 1991 reported that Trichosanthin exert deleterious effects on reproduction and is a clinical medicine for abortion and they carried out their experiment on a mouse. In fertilized animals, TCS causes necrosis of the syncytiotrophoblasts of placental villi, and results, the embryo fails to develop[19]. The anti-tumor effects of TCS were first tested on the cells of choriocarcinoma and malignant trophoblastic cancer. About two decades ago, Dai and colleagues conjugated colloidal gold to TCS molecules and found that TCS specifically entered cultured trophoblast and choriocarcinoma JAR cells via receptor-mediated endocytosis. The LDL receptor-related protein-1 (LRP1) has been suggested as a major receptor for phagocytosis of TCS in cultured JAR and BeWo cells, which might be the molecular basis of the abortifacient and anti-choriocarcinoma activities of TCS[19,20]. Influx of calcium and production of reactive oxygen species (ROS) were also observed as well in TCS-treated JAR cells, and ROS production might be a consequence of calcium ion signaling[21].

In the year 2010, Wang *et al* investigated that Trichosanthin induces Apoptosis by its activity[15]. Apoptosis is a form of cellular suicide that ensures that super fluous or harmful cells are eliminated from multi-cellular organisms. Apoptosis is distinguished from necrosis through characteristic morphological and biochemical changes, including compaction and fragmentation of the chromatin, plasma membrane blebbing and cell shrinkage. Apoptosis is mechanism in which activation of certain types of proteases, nucleases, and

cytoskeleton breakdown. Apoptosis begins with the condensation of nuclear chromatin at the nuclear periphery, followed by blebbing of the nuclear and cytoplasmic membranes, culminates in the fragmentation of residual nuclear structures into discrete membrane-bounded apoptotic bodies in sequential manner. Apoptosis occurs in many different cell types and in response to diverse stimuli. Apoptosis is now considered to be an essential cellular response to agents used for anti-tumor chemotherapy and radiotherapy.

Trichosanthinstimulates the production of ROS in JAR cells and that ROS are involved in the TCS-induced apoptosis of JAR cells. TCS treatment induced a transient elevation of intracellular calcium and a slow rise of ROS in human chronic myeloid leukemia cell line K562[17] was noticed. It was observed that calcium chelators and antioxidants did not have a conspicuous effect on TCS induced apoptosis, suggesting that calcium changes and ROS may not be implicated in TCS-mediated apoptosis in K562 cells. In contrast, TCS elicited an increase in cytosolic calcium and induced apoptosis in HeLacell. In the year 2009, Wang et *al*., confirmed that this apoptotic cell death can be reduced by a specific calcium chelators and ethylene glycol bis (2-aminoethyl) tetra (acetoxymethyl Ester) (EGTA-AM). Therefore mentioned discrepancies may be ascribed to the different types of cells studied[22]. TCS may induce apoptosis via distinctly different mechanisms in different cells. In other cell line JAR, TCS stimulated the production of ROS, which can be inhibited by the superoxide radical anion ($O2^{--}$) scavenger superoxide dismutase, the H_2O_2 scavenger catalyses, and the hydroxyl radical (OH-) scavenger mannitol. The antioxidant Trolox and an inhibitor of metal-facilitated OH- formation, diethylene-triaminepenta acetic acid, also markedly inhibited TCS induced cell death.

All these results O_2-, H_2O_2 and OH- indicate that are involved in TCS-induced ROS formation in JAR cells. In addition, TCS-induced activation of caspase 3 was initiated within 2 h; however, TCS-induced production of ROS was initiated within 5min. These findings suggest that the production of ROS precedes the activation of caspase 3.Thus the ROS is involved in the TCS-induced apoptosis of JAR cells may provide new insight into the anti-tumor and anti-HIV mechanism of TCS.

TCS administration induced up regulation of the protein chaperone BiP, transcription factor CHOP and also activated caspase 4 in HeLa-60 cells, which for the first time strongly supported the involvement of ER stress pathway in TCS-induced apoptosis[17]. On the other hand, inducible nitric oxide synthase (iNOS) mRNA expression and protein levels were elevated in cells treated with TCS and nitric oxide (NO) production by cells was augmented in the presence of TCS. When L-NIL, the specific inhibitor of iNOS was added to suppress NO production induced by TCS, OVA-specific cell death was significantly inhibited; meanwhile, cellular thymidine incorporation was restored to normal levels. These observations suggest that TCS could suppress antigen-specific T cell activation via an NO-mediated apoptosis pathway. TCS can induce specific changes of cytoskeleton configuration associated with the attenuated expression level of actin and tubulin genes in apoptotic HeLa cells[23] successfully.

In the year 2012, Fang*et al*reported that TCS can induce apoptosis especially in breast tumor cells. Breast cancer ranks as a common and severe neoplasia in women with increasing incidence as well as high risk of metastasis and relapse.TCS manifested anti-proliferative and apoptosis-inducing activities in both estrogen-dependent human MCF-7 cells and estrogen-independent MDA-MB-231 cells.

As the accumulation of cells in sub-G1 phase is indicative of cell death. TCS treatment slowly increased the number of apoptotic cells in MCF-7 cells. Similarly in MDA-MB-231 cells, the number increased in TCS-treated groups compare to non-treated group. Furthermore, TUNEL assay was applied to detect DNA fragmentation and the data showed that more cells were undergoing DNA fragmentation after TCS treatment in both MCF-7 cells and MDA-MB-231 cells.TCS-treated cells nuclear morphological changes visualized by staining the cells with Hoechst 33342 dye. In MCF-7 cells, exposure to TCS caused typical morphological changes of apoptosis, such as karyorrhexis, significant nuclear condensation and fragmentation compared with the non-treated group. This type of phenomenon was also observed in TCS-treated MDA-MB-231 cells[24].

Fang *et al* in the year 2012 reported that Trichosanthinactivate caspase-mediated apoptosis in breast cancer cells[28]. Apoptosis always executed in caspase-8-regulated plasma membrane extrinsic pathway and/or caspase-9-regulated cell damage intrinsic pathway[25]. Immuno-blotting analysis indicated that TCS treatment resulted in a dose-dependent activation of the initiator caspases 8, 9 and the executor caspase 3.And those were followed by proteolytic cleavage of PARPs shown in the right panel of normalized expression levels of remaining caspases 8, 9 and 3 were decreased compared with control in assay. Accordingly, there were increased levels of both activated caspase-8 and caspase-9 in TCS-treated group compared with control.

Three breast cancer cell lines, including two estrogen-dependent breast cancer cell lines are MCF-7 cells, highly metastatic BT-474 cells and estrogen-independent MDA-MB-231 cells were employed in Fang et *al*., study. Trichosanthin inhibited cell viability in all three tested cell lines in the following ranking of potency: MDA-MB-231>MCF-7>BT-474 cells. It was revealed that TCS exhibited both cytostatic and cell-death inducing activities which in turn contributed to the inhibition of cell viability in both types of breast cancer cells. This cytostatic activity was at least partially contributed by cell cycle arrest. It seems that TCS can induce G1 phase arrest in breast cancer cells as it did in human lung cancer A549 cells.

Fang*et al*, in the year 2012 carried out investigation on the effect of TCS on some G1 cell cycle-regulating proteins, such as cyclin D1 and phosphor-Rb are warranted[27]. Furthermore, flow cytometric analysis using Annexing V/PI showed that TCS could dose-dependently induce in early apoptosis and late apoptosis in both MDA-MB-231 and MCF-7 cells. In accordance with this, stereotypical apoptotic features were noticed; these include karyorrhexis, chromatin condensation and inter nucleosomal DNA fragmentation. The results were reminiscent of the action of other natural chemotherapeutic components toward breast cancer cells. For instance, the ribonuclease from *Momordica charantia* seeds (RNase MC-2) manifested the same effects on MCF-7 cells. Caspases are the principal effectors of apoptosis involved in pathways such as caspase-8-regulated extrinsic and caspase-9-regulated intrinsic pathways. The caspase-9 pathway links mitochondrial damage to caspase activation and serves as an index of damage in mitochondrial membrane function.

The antitumor efficacy of TCS in *invivo* systems were substantiated by results from MDA-MB-231 bearing nude mice. Every other day, Trichosanthinwas administered intra peritoneal at a dose of 5.0 mg/kg body weight regularly. Compared with control, Trichosanthintreatment abated both tumor volume as well as tumor weight from the 6th day of treatment constantly. This antitumor effect correlated with increased levels of apoptosis in the tumors

of TCS-treated group, as supported by the increase of activated caspase-3, cleaved PARP, and DNA fragmentation (TUNEL-positive cells). Interestingly, necrosis was also detected in TCS-treated group compared to the control group. This infers that reduction of tumor proliferation by induction of apoptosis is a mechanism of the *invivo* antitumor activity of TCS toward MDA-MB-231 xenograft. Protein engineering studies on TCS, such as PEGylation and the construction of immuno-toxin, might help to increase its drug specificity as well as reduce its side effects[28].

Lee-Huang*et al*, in the year 2000 reported that MAP30 inhibited cell proliferation and the expression of HER2 in MDA-MB-231 cells[29]. More importantly, treatment of MDA-MB-231 bearing SCID mice with TCS in dose EOD for a total of ten injections, resulted are effective and impressive i.e pronounced prolongation of survival and nearly one quarter of the mice remained tumor-free for 96 days. The above mentioned MCL was also active *invivo* in a CNE-2 xenograft tumor model. It inhibited tumor growth by inducing apoptosis of tumor cells. TCS manifested cytotoxicity in both MDA-MB-231 cells and MCF-7 cells.

In Fang *et al*(2012) study TCS was administered intraperitoneal at a dose of 5.0 mg/kg body weight regularly. The dose applied was acceptable since the mice did not lose weight during the course of treatment. Recently, a large clinical study has indicated that TCS was effective against ectopic pregnancy in 140 women at the dosage of 1.8 mg for each person using intramuscular injection. There no significant side effects were observed for most of the patients and it seems there was no side effects o on their subsequent pregnancy as well as giving birth to a healthy baby[30].

Final conclusion of the Fang*et al*. (2012) report TCS manifested the ability to induce apoptosis in both estrogen-dependent MCF-7 cells and estrogen-independent MDA-MB-231 cells in *invitro* and/ or *in vivo* experiments. Proteolytic processing of initiator caspases as well as executor caspase and subsequent spawned apoptosis contributed to TCS-induced apoptosis. Besides the function as an abortifacient, application in the treatment of hydatidiform moles and invasive moles, Trichosanthin may provide a plethora of treatments or even for the development of a novel therapy combined with other chemotherapeutic measures for both estrogen-dependent and independent breast cancers. The most important thing that has been noticed in clinical studies on the application of TCS against other human diseases showed that it was effective, the effective dose level was safe, relatively well tolerated, through with some acceptable mild side effects[31,32].

Thus TCS was found to be active against a variety of tumors including cervical cancer, choriocarcinoma, leukemia/lymphoma, stomach cancer, colon cancer, hepatoma, breast cancer, and prostate cancer. The toxic mechanisms of Trichosanthin tumor cells include inhibition of the proliferation and induction of apoptosis of tumor cells, and the detailed mechanism varies in different tumor cells.

Cardio protective Activity

Shah *et al*., in the year 2012 reported that methanol extract of fruit of *Trichosanthes cucumerina* effective in doxorubicin-induced cardio toxicity in rats. Cardiovascular disease is caused by disorders of the heart and blood vessels, and includes coronary heart disease (heart attacks), cerebrovascular disease (stroke), raised blood pressure (hypertension), peripheral artery disease, rheumatic heart disease, congenital heart disease and heart failure. The major reasons of cardiovascular disease are tobacco use, physical inactivity, an unhealthy diet and harmful use of alcohol Doxorubicin (DOXis toxic agent for all

cellular components; Adriamycin) which is used as antitumor drug for treating several types of solid cancer, leukemia and lymphomas. *T. cucumerina* contains many different antioxidant components that provide protection against harmful free radicals that are strongly associated with reduced risk of cardiovascular diseases[33].

Antiulcer Activity

Kannan*et al*., (2011) investigated the gastro protective effect of *Trichosanthes tricuspida*against ethanol induced gastric ulceration on albino rats and it was observed that reduction in ulcer, index shows the ability of the extract either to protect the gastric mucosal (cytoprotective) against ulceration or may be suppression of already established ulcers. Hexane extract and chloroform extract have more gastro protective activity as compare toaqueous and ethanol extract. It concludes that the active constituent responsible for gastro protective activity is Polar in nature and also investigated the antioxidant properties[34].

Antidiabetic activity

In the year 2009, Arawwawala *et al.,*investigation demonstrate that the HWE (Hot Water Extract) of *Trichosanthes cucumerina* aerial parts can significantly reduce the blood glucose levels and improve the glucose tolerance of norm glycemic and STZ–induced diabetic rats. The increased levels of serum glucose in STZ–induced diabetic rats were lowered constantly by *T. cucumerina* extract administration. It also suggests that HWE may act as an insulin secretagoue and/or sensitize insulin receptors, as proposed for some plant extracts and some sulphonylurea.Results obtained in the *Arawwawala et al*., study provide supportive evidence for the view that *T. cucumerina* exerts its hypoglycemic action by mechanisms similar to those of sulphonylureas[35].

Antibacterial Activity

At Arawwawala*et al.,* (2011) study reveals that *Trichosanthes cucumerina* has components that can exert significant antibacterial activity against *S. aureus, S. pyogenes, E. coli* and *P. aeruginosa* that are known well as wound pathogens. The CEE (Cold Ethanol Extract) can exert consistently better antibacterial activity than the HWE. This difference in activity of the HWE and CEE may be related to the polarity of antibacterial compounds presents. Both *E. coli* and *P. aeroginosa* were found to be more susceptible than *S. aureus* and *S. pyogenes* to the action of the *T. cucumerina* extracts. This is possibly due to the differences in chemical composition and structure of cell wall of the microorganisms. In result, *Trichosanthes cucumerina* extracts exhibited antibacterial activity against both gram (+) ve bacterial strains such as *S. aureus*, *S. pyogenes* and gram (-) ve bacterial strains such as *E. coli* and *P. aeroginosa* mediating the presence of a broad spectrum of antibacterial compounds in the plant[36].

Hepatoprotective

Aiyalu Rajasekaranand Muthusamy Periyasamy (2012) reported the Hepatoprotective effect of Ethanolic Extract of *Trichosanthes lobata* (EETL). Hepatotoxicity is a common cause of severe metabolic disorders and even death. The EETL exhibits protective activities against paracetamol-induced Hepatotoxicity. Flavonoids exhibit vasoprotective, anti-inflammatory, anti-allergic, antimicrobial, antioxidant, Hepatoprotective, anti-osteoporotic, and anti-neoplastic properties. On administration of EETL and paractamol silymarin group, the serum markers were restored to the normal levels.

Histopathological studies of rats administered paracetamol showed severe necrosis and disappearance of nuclei. This could be due to the formation of highly

reactive metabolites (e.g. NAPQI), because of excessive administration of paracetamol. All these histopathological changes were significantly reduced in rats treated with EETL. The study of serum markers such as AST, ALT, ALP, and bilirubin, and total protein were found to be of great value of assess to clinical and experimental liver damage. Pretreatment with *T. lobata*, significantly attenuated elevated levels of serum markers.Thus Ethanolic Extract of*T. Lobata* conditions the hepatocytes so as to protect the integrity of the membrane from paracetamol-induced leakage of serum markers into circulation. Plants most commonly used to treat liver disorders are *Curcuma longa* (turmeric), *Glycyrrhizin glabra* (licorice) and *Camellia sinensis* (green tea), and they are all reported to be Hepatoprotective[37].

Larvicidal activity

Sonwalkar*et al.,* (2013) investigated and revealed that the fruit of *Trichosanthes tricuspidata* has new mosquitocidal compound against the mosquito *Culexquinquefasciatus*Say.*Culex*is a genus of mosquito, and is important in that several species serve as vectors of important diseases, such as West Nile virus, filariasis, Japanese encephalitis, St. Louis encephalitis and avian malaria. *T. tricuspidata* was used to study the mortality of the mosquito *C. quinquefasciatus.* Larvicidal Bioassay method was used, these extract was divided into two parts i.e. Methanol Fruit Extract (MFE) & Petroleum Ether Fruit Extract (PEFE) was prepared. Both showed good mortality but highest larval mortality was found in MFE. The MFE of *T. tricuspidata*may have potential to develop as natural larvicidal agent[38]. This plant can be used as natural mosquito repellent, which may be useful in the household to kill mosquitoes, mice, etc.

Anti-inflammatory activity

Fulzule*et al*(2001) studied anti-inflammatory activity of *Trichosanthes cucumerina*and it was evaluated by use of the carrageen an-induced paw edema model in Wistar rats. In addition, the mechanism by which *T. cucumerina* mediated the anti-inflammatory activity was assessed by determining its effects on membrane stabilizing activity and nitric oxide inhibitory activity. Inhibition of nitric oxide (NO) production and membrane stabilization activities are probable mechanisms by which *T. cucumerina* mediates its anti-inflammatory actions. These findings rationalize the traditional usage of this plant as an anti-inflammatory agent and membrane stabilizing properties and no inhibitory activity are possible mechanisms through which *Trichosanthes cucumerina* mediates its anti-inflammatory action[39].

Antioxidant activity

In MukeshTanwar*et al*.,(2011) reported that *Trichosanthes dioica Roxb* contains possess antioxidant activityi.e. due to its free radical scavenging activity and its ability to reduce elevated levels of serum marker enzymes which may be due to presence of Antioxidants(such as vitamin C, Beta carotene, carotene, saponins and tannins).Antioxidants plays an important role to protect the human body against damage by reactive oxygen species. Ascorbic acid may have counteracted the free radicals through effective scavenging and blocking the conjugation of reactive metabolite to GSH. The levels of vitamin C and E were significantly depleted in paracetamol intoxication which may be due to excessive utilization of quenching the enormous free radicals produced during paracetamol intoxication[40].

The antioxidant potential of *Trichosanthes dioica* was assessed by DPPH assay and H_2O_2 method. The DPPH assay is

based on the measurement of scavenging ability of antioxidants towards the stable radical DPPH. Antioxidants reduce the radicals to the corresponding hydrazine when it reacts with the hydrogen donor in the antioxidant principles. DPPH radicals react with suitable reducing agent, the electrons become paired off and the solution losses colourstoichiometrically depending on the number of electrons taken up. Hydrogen peroxide concentration is decreased by scavenger compounds and therefore absorbance value also decreases. Antioxidant shows good scavenging activity against H_2O_2 and DPPH free radicals. *Trichosanthes dioica* extracts show reduction in absorbance value in DPPH assay and H_2O_2 method, which might be due to radical scavenging activity of vitamin C and carotene.

Antifertility Activity

In the year 2009, Kage *et al.,* investigated the antifertility activity in albin rats with treatment of the Ethanol Extract of *Trichosanthes cucumerina* L. var. *cucumerina*(EETC)showed a significant increase in the duration of estrous cycle with prolonged estrus and metestrus phases and decrease in diestrus and proestrus phases. The difference in the duration of estrous cyclicity between the control and the treatment groups is attributed to the vaginal cornification, influenced by the more estrogen production by the extract which is estrogenic in nature. Investigation suggested that the level of cholesterol significantly increased in the ovaries which are treated with EETCare clearly defines the role of gonadotropins in consuming cholesterol for steroid hormone biosynthesis within the ovary. And also the alternative effect of this drug upon cholesterol utilization enzymes like 3b HSD and 17b HSD to synthesize steroid hormones cannot be ignored. This effect is reflected in drastic decrease in the enzyme activities of ovaries after treatment with high dose of EETC. Ethanol Extract of whole plant of *Trichosanthes cucumerina* L. var.*cucumerina* reduced the serum levels of gonado-tropins, might have affected folliculogenesis and steroidogenesis in ovary[44].

Anti-herpetic activity

Zheng *et al,* in the year 2001 noticed that the Anti-herpetic activity of Trichosanthin can be enhanced by acyclovir and interferon. It was clearly demonstrated that TCS is active against herpes simplex virus (HSV) and its efficiency is similar to acyclovir (ACV) on a molar basis. Toxicity of TCS varies between cell types, for example, choriocarcinoma is much more sensitive to TCS than hepatoma. In Zheng *et al* study they used Vero cells as hosts and the synergistic effect of TCS with two other anti-viral agents namely ACV and INFs were investigated. ACVis commonly used for treatment of HSV infection which targets viral DNA polymerase after being phosphorylated by HSV-specific thymidine kinase and at the only presence of infected cells it was being activated. The other anti-viral agent is interferons (INFs). Its action depends on the kind of INF and the type of cells.

It had known that treatment of HSV-infected cells resulted in a decrease of ribonucleotide reductase leading to a fall in the size of deoxyribonucleotide pools. Outcomes clearly demonstrated that ACV or INF enhanced the anti-viral action of TCS. In the presence of a fixed low dosage of either ACV or INF that has no significant anti-viral effect, the potency of TCS was enhanced by over 100-fold. It wasalso noticed that all RIPs are not capable of anti-viral activity. The anti-viral action of protein is due to selective inhibition of DNA synthesis. But it can be speculated that the antiviral mechanism of TCS should not be the same as that of ACV or INF mechanisms. Alternatively, if the

mechanisms were the same, the synergistic effect would have been summative rather than 100-fold potentiated as found in Zheng *et al*study.TCS is active against HSV and this action can be potentiated by ACV or INF[45].

OTHER ACTIVITIES

CHOLESTEROL-LOWERING ACTIVITY

Sharmila *et al* (2007) observed cholesterol lowering activity of the aqueous fruit extract of *Trichosanthes dioica Roxb.* In normal and streptozotocin diabetic rats. The influence of alcoholic extract of whole fruit of T. dioica on blood sugar, serum lipids, lipoproteins and faecal sterols in normal albino rabbits. Effect of oral administration of alcoholic extract of whole fruit of *Trichosanthes dioica Roxb* with basal diet for four weeks was studied in the normal albino rabbits. It was observed that this extract lowered the blood sugar, total cholesterol, low density lipoprotein cholesterol and triglyceride levels, and increased the high density lipoprotein cholesterol, phospholipids and faecal sterol levels[41].

IN SKIN DISORDER

In the year 1999, Bhujbal showed that polyhebral formulation including T. dioica is useful in skin disorder. Bhujbal investigated about fifty cases of various skin diseases were treated with decoction of a mixture of *Trichosanthes*& other herbal crude drugs in a dose of 20ml to 40ml empty stomach with hot water & honey for 4 to 6 weeks. It was observed that the drug was found to be useful and no side effect was observed[42].

WOUND HEALING ACTIVITY

In Periyanayagam *et al* (2014) demonstrated that *Trichosanthes cucumerina* has the ability to repair the wound and leaves of this plant used as alexiteric, astringent, diuretic and emetic. Wound healing is the process of repair that follows injury to the skin and other soft tissues. Following injury an inflammatory response occurs and the cells below the dermis begins to increase collagen production. Later the epithelial tissue is regenerated. Wound healing management is a complicate and expensive one.

*Trichosanthes cucumerina*contains Flavonoids fraction using ex-vivo porcine skin wound healing model (PSWHM)[43]. Plant phenolics act as primary anti-oxidants or free radical scavangers and its derivatives were reported to be effective against viruses, bacteria and fungi, and many diseases including wound healing effectively. Lipid peroxidation is an important process in burns, wounds and skin ulcers. Collagen fibrils viability increases by inhibiting lipid peroxidation which cause increases the strength of collagen fibers. Finally it prevents cell damage and promotes DNA synthesis. Therapeutically potential phenolic compounds possesses anti-infective, anti-inflammatory, decreasing level of lipid peroxidation which improve vascularity, increase collagen synthesis and promotes cross linking of collagen. The present findingprovides scientific evidence to ethno medical properties of *Trichosanthes cucumerina* leaves in wound healing property[43].

CONCLUSION

*Trichosanthes*species contains significant protein known as ribosome inactivating protein (RIP). RIP play a significant role in developing formulations for geriatric care as it is having almost all the properties of pharmaceutical care. As a result it is effectively used for the cure of minor skin diseases to life threatening cancers and HIV. RIP protein helps in formulation of anticancer agents. Effect of RIP on various cancer lines includes

Carcinoma, leukemia/lymphoma, tumor cell, cervical, choriocarcinoma, breast tumor cells. RIP is active against these cell lines either by inhibition or by Apoptosis.It can be also used against free radicals, heart diseases, liver disorders, ulcers, diabetes, cholesterol and skin disorders. *Trichosanthes*species are also good potential sources of antioxidants and minerals.

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Table 1. Type of *Trichosanthen species*, General name and respective activities are tabulated below

S.no	*Trichosanthes species*	General name	Activities
1.	*Trichosanthes cucumerina*	Snake gourd (var. *anguina*), Serpent gourd, Chichinga, and Padwal	Anthelmintic, Antidiarrhoeal, anti-inflammatory, Anticancer agent, larvicidal effects, Antidiabetic, cardio protective, Antibacterial, wound healing, Antifertility activities.
2.	*Trichosanthes dioica*	Gourd Parwal (Hindi) Paror(Maithili). *Green potato*(India)	Type-II ribosome inhibitory proteins (Type-II RIP), Anti proliferative, Anticancer agent, Antioxidant, Anti-Cholesterol activity, in skin disorder
3.	*Trichosanthes kirilowii*	Chinese cucumber	Anti-HIV type I ribosome-inactivinglectinAntitumor promoters, Antiulceractivity
4.	*Trichosanthes tricuspidata*	*LalIndrayan*(Hindi); Redball snake gourd (English); *Kalayar*(Malaya); *Kaundal(*Marathi*); Avuduta*(Telugu); *KheKaDaeng*(Thai); and *Indreni*(Nepal);	Anti Larvicidal activity
5.	*Trichosanthis ra dix*	Tianhua fen (Mandarin)	Relieves pyreticosis, polydipsia, swelling and ulcer, RIP, Anti-hepatitis B virus
6.	*Trichosanthes lobata*	-------	Hepatoprotective effect, Anti-malarial agent.