"ANTITUMOR ACTIVITY OF THE LEAVES OBTAINED FROM *STROBILANTHES CONSANGUINEUS*"

The Tamil Nadu Dr.M.G.R Medical University Chennai

In partial fulfilment of the degree of

MASTER OF PHARMACY

(Pharmacology)

Submitted by

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CERTIFICATES

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1.0 INTRODUCTION

Cancer has been a constant battle globally with a lot of development in cures and preventative therapies. The disease is characterized by cells in the human body continually multiplying with the inability to be controlled or stopped. forming tumors. Current treatments include chemotherapy, radiotherapy and chemically derived drugs. Treatments such as chemotherapy can put patients under a lot of strain and further damage their health. Therefore, there is a focus on using alternative treatments and therapies against cancer. For many years herbal medicines have been used and are still used in developing countries as the primary source of medical treatment. Plants have been used in medicine for their natural antiseptic properties. Thus, research has developed into investigating the potential properties and uses of terrestrial plants extracts for the preparation of potential nanomaterial based drugs for diseases including cancer.

Multiple researchers have identified species of plants that have demonstrated anticancer properties with a lot of focus on those that have been used in herbal medicine in developing countries Compounds which are characteristic to the plant kingdom and are necessary for plant survival and “housekeeping” of the organism are being investigated for their ability to inhibit growth and initiate apoptosis of cancerous cells. This article aims to take an overview of current plant derived compounds that have anticancer therapeutic properties and their developments in the field. Globally cancer is a disease which severely effects the human population. There is a constant demand for new therapies to treat and prevent this life-threatening disease. Scientific and research interest is drawing its attention towards naturally-derived compounds as they are considered to have less toxic side effects compared to current treatments such as chemotherapy. The Plant Kingdom produces naturally occurring secondary metabolites which are being investigated for their anticancer activities leading to the development of new clinical drugs. With the success of these compounds that have been developed into staple drugs for cancer treatment new technologies are emerging to develop the area further. New technologies include nanoparticles for nano-medicines which aim to enhance anticancer activities of plant-

derived drugs by controlling the release of the compound and investigating new methods for administration. This review discusses the demand for naturally-derived compounds from medicinal plants and their properties which make them targets for potential anticancer treatments. Several naturally produced herbal formulations are currently available for cancer patients.

Therefore scientific consideration and test of traditionally used herbs for the treatment of different malignancies could be also considered as a very valuable source for new chemotherapeutic drugs.(2) A number of studies carried out over the last few decades on prevention and treatment of HCC have led to the identification of several herbal compounds and formulations that can affect the initiation, promotion as well as the progression processes of HCC. The most important active constituents of the Aloe plants were anthraquinones like aloin, barbalion, anthranol, cinnamic acid, aloetic acid, emodin, chrysophanic acid, resistanol, and enzymes (including cyclooxygenase and bradykininase), together with Other compounds such as vitamins, saccharides, and amino acids(3) It was reported that the other anthraquinones of Aloe plants had mutagenic and genotoxic effects in bacterial and mammalian test systems the genotoxic effects were illustrated in present research by DNA damage assay and Real Time-PCR. The antitumor activity of 50% ethanol extract (100 mg/ kg) of A. vera was evaluated by Bharath against Ehrlich ascites carcinoma tumor in mice. Ethanol extract of A. vera exhibited antitumor effect by modulating lipid peroxidation and augmenting antioxidant defense system in Ehrlich ascites carcinoma bearing mice Also, Aloe-emodin is one of the active components in the leaves of A. vera which revealed anticancer and cytotoxic activities against neuroectodermal tumors, lung squamous cell carcinoma and hepatoma cell .C. comosum also, has been exhibited anti- inflammatory, anti-ulcer and anti-cancer activities in rat and shrimp animals model Dehydrodicatechin A is an active component of C. comosum which inhibits the growth of Ehrlich ascites(5) Abdel-Sattar et al showed that C. comosum methanolic and aqueous extracts ameliorated haloperidol induced neuro- and hepatotoxicities in male Albino rat. In our study, we have noticed that the cytotoxic activity of A. vera and C. comosum might be through modulation of apoptosis, there for both extracts demonstrated antitumor effects against HepG2 cells. Gene and

protein expressions of both p53 and Bcl2 were significantly altered in response to extracts. Up-regulation of expression of p53 and down-regulation of Bcl2 in a time and dose dependent manner were evident in the human HCC cell line which is a major pathway for regulation of programmed cell death. Both extracts could have cytotoxic and genotoxic activity. C. chromosome showed a higher level in inducing morphological changes associated apoptosis, DNA damage, gene and protein expressions. HeLa cervical cancer cells, and NLE shows proliferation inhibitory effects in prostate cancer cells. Interestingly, the androgen-dependency status fails to modulate anti-proliferative effects of NLE in prostate cancer cells

For example, neem extract disrupts proliferation of both androgen-dependent and -independent prostate cancer cells .Since androgen-refractory prostate cancer cells are more resistant to apoptosis and lead to prostate cancer recurrence, treatment with active components of neem may provide therapeutic benefits to patients with recurrent prostate cancer. Similar to lack of androgen dependency, the anti-proliferative effects of neem are consistent in both estrogen-dependent and -independent breast cancer cells . Cell cycle progression is tightly controlled by a complex network of regulatory proteins including cyclins, cyclin-dependent kinases (CDKs), CDK inhibitors (CKIs), cell cycle checkpoint proteins, and transcription factors such as E2F.Studies on the effects of neem or its components on cell cycle and proliferation of tumor cells have identified multiple target proteins. For example, treatment of HeLa cells with azadirachtin decreases the levels of cyclin B and cyclin D1, and induces the expression of CKI p21, which collectively led to G0/G1 cell cycle arrest .Analysis of cell cycle distribution in nimbolide-treated colon carcinoma cells revealed that this active neem component induces both G0/G1 and G2/M arrest accompanied by alterations in cyclins, CDKs and CKIs Additional nimbolide targets for G2/M cell cycle checkpoint proteins are CHK2 and Rad17 . Although detailed mechanisms are unknown, nimbolide disrupts cell cycle progression, and thus inhibits proliferation of HeLa breast cancer ,choriocarcinoma , lymphoma leukemia and melanoma cells.. Additional neem components that have been characterized show similar suppressive effects on the growth and proliferation of tumor cells. For example, treatment with NLE or neem-derived gedunin decreases proliferation of

pancreatic or ovarian cancer cells, respectively. The subsets of differentially regulated genes induced by gedunin, identified by bioinformatics analysis, encode proteins involved in cell cycle control as well as other cellular processes. Interestingly, the combination of gedunin and cisplatin further decreases the proliferation of treated ovarian cancer cells by almost 50% compared to the cells treated with cisplatin alone. These findings suggest the possibility that gedunin and other potential neem components could enhance the efficacy of chemotherapeutic agents, and such combinatorial therapy may offer additional benefits. In vivo studies of neem extracts or components show significant anticancer properties, confirming the clinical relevance of the in vitro findings. NLE inhibits the process of carcinogenesis in carcinogen 7,12-dimethylbenz[a]anthracene (DMBA)- induced HBP mouse model, which is accompanied by decreased expression of proliferating cell nuclear. The effects of neem components on cancer cell death Besides inhibiting cancer cell proliferation, neem components exert anticancer effect by induction of apoptosis as well as other forms of cell death including autophagy. Extracts from seeds and leaves of neem induce apoptosis in different types of cancer cells such as leukemia, prostate cervical, colon , stomach , and breast as well as choriocarcinoma , and hepatocarcinoma cells . These findings suggest a proapoptotic effect of neem extracts on a broad spectrum of cancer cell types. Author Manuscript Author Manuscript Author Manuscript Similarly, the administration of individual neem components also induces cancer cell death. For example, nimbolide induces apoptosis in breast cancer , prostate cancer , hepatocarcinoma , cervical cancer, choriocarcinoma , colon cancer , lymphoma, leukemia, and melanoma cells . Azadirachtin shows similar effect in cervical cancer cells. An increasing number of less-characterized limonoids that have been recently isolated from different parts of neem also exhibited proapoptotic effects in leukemia and stomach cancer cells Consistent with the anti-proliferative effects of neem, its proapoptotic potentials are not affected by the hormonedependent status in prostate cancer and breast cancer cells Apoptosis occurs through the intrinsic mitochondrial pathway or the extrinsic pathway mediated by membraneassociated death receptors . Neem limonoids induce apoptosis through the intrinsic pathway in prostate cancer and cervical cancer cells, accompanied by increased release of

cytochrome c from mitochondria. The mitochondrial release of cytochrome c is one of the initiating events during apoptosis via intrinsic apoptotic pathway . This cytochrome c release is regulated by proapoptotic members (e.g. Bax and Bad) and antiapoptotic members of the Bcl-2 family (e.g. Bcl-2 and Bcl-xL). Thus Bcl-2 family proteins are important targets for exerting anticancer effects of neem in cancer cells. For example, neem-induced apoptosis in prostate cancer cells is mediated by the concurrent decrease of Bcl-2 and increase of Bax levels . In addition, treatment with individual component nimbolide induces expression of Bad and Bax in breast cancer cells, while decreases the levels of Bcl-2 and Bcl-xL [20]. Similar pattern of modulation of Bcl-2 family proteins has also been observed upon nimbolide or azadirachtin exposure to cervical cancer cells, and in nimbolide treated choriocarcinoma cells [26].

Nimbolide and azadirachtin also induce expression of caspases while suppress antiapoptotic protein survivin in cervical cancer cells . In addition to the well-characterized neem components, a newly-isolated neem limonoid, 2,3-dihydro3α-methoxynimbolide, shows proapoptotic effects in stomach cancer cells through modulation of caspase activities accompanied by modulation of the ratio of Bax/Bcl-2 protein levels . These findings demonstrate that neem components exert anticancer effects by modulating Bcl-2 family proteins, caspases, and additional regulatory proteins. Apoptosis or cell death is a very complex process involving multiple groups of protein, thus targeting multiple components in the apoptotic pathway is likely to improve the anticancer efficacy of neem components or extracts. Interestingly, neem-induced apoptosis occurs through a p53-independent mechanism in colon cancer cells, as loss of p53 fails to prevent neem-induced apoptosis. Anticancer Properties: Fu Y, et al, investigated Licochalcone (LA) elicited growth control and induction of apoptosis using androgenindependent p53-null PC-3 prostate cancer cells. The findings of this study were-1) LA induced modest level of apoptosis but had more pronounced effect on cell cycle progression arresting cells in G2/M, accompanied by suppression of cyclin B1 and cdc2. 2)It also inhibited phosphorylation of Rb, specifically phosphorylation of S780 with no change of phosphorylation status of T821,3) decreased expression of transcription factor E2F concurrent with reduction of

cyclin D1, 4)down-regulated CDKs 4 and 6, but increased cyclin E expression. These findings provided explanation for LA activity and suggested that it might be considered as a chemopreventive agent. Kanazawa M, et al investigated the anti-tumor effect of isoliquiritigenin on prostate cancer in vitro. They used DU145 and LNCaP prostate cancer cell lines as targets. In this study, the effects of isoliquiritigenin on cell proliferation, cell cycle regulation and cell cycle-regulating gene expression were studied. The effects of isoliquiritigenin on the GADD153 mRNA and protein expression, and promoter activity were also investigated. The researchers of this study found that isoliquiritigenin significantly inhibited the proliferation of prostate cancer cell lines in a dose-dependent and time-dependent manner. Fluorescence-activated cell sorting (FACS) analysis indicated that isoliquiritigenin induced S and G2/M phase arrest and that isoliquiritigenin enhanced the expression of GADD153 mRNA and protein associated with cell cycle arrest. They have concluded that isoliquiritigenin was a candidate agent for the treatment of prostate cancer and GADD153 might play an important role in isoliquiritigenin-induced cell cycle arrest and cell growth inhibition.

The anticancer activity of turmeric when evaluated prophylactically and therapeutically i.e., pre-induction treatment and post -induction treatment respectively, by two different routes of administration i.e., per oral and topical application. Though post-induction per oral treatment with turmeric demonstrated a significant anticancer activity against MNU-induced mammary cancer in rats, the degree of anticancer activity was more prominent in prophylactic treatment groups and was more effective particularly with topical application. It was clearly evidenced by the decreased drastic reduction in mean tumor volume and higher degree of tumor growth inhibition in prophylactic topical application of turmeric when compared to the therapeutic treatment of groups. Our study demonstrated similar results with the previous work reported . Prophylactic topical application of turmeric has shown superior efficacy when compared to all other groups in reduction of the incidence rates of tumor induction, prolongation of mean latency periods of tumor development, reversal of mean tumor volume and inhibition of tumor growth. Hence, interesting findings in this study are i) Preventive role of turmeric against MNU induced

mammary cancer was more predominant than the therapeutic role of turmeric on MNU induced mammary cancer. ii) Preventive role of turmeric was more pronounced with topical application though it has demonstrated moderate prophylactic effect with per oral administration of turmeric. In an in-vivo study, dietary administration of 1% turmeric, 0.05% ethanol extract of turmeric, when administered during initiation and post initiation periods significantly inhibited the 7, 12 – dimethyl benz (a) anthracene (DMBA) induced mammary tumorigenesis by reducing tumor multiplicity, tumor burden and tumor incidence. Simultaneous administration of 1% curcumin-free aqueous turmeric extract as the sole source of drinking water during the initiation phase did not suppress DMBA-induced mammary tumorigenesis but suppressed the DMBA-induced mammary tumorigenesis when administered during post initiation period by reducing tumor multiplicity and tumor burden but not the tumor incidence. Till date, there was no evidence of anticancer activity with topical application of turmeric in breast cancer model.

In two & in vivo studies reported earlier, topical application of 100 or 3000 nmol curcumin in CD-1 mice and 0.2% or 1% curcumin in diet significantly reduced the tumor incidence and tumor volume in dimethyl benz (a) anthracene (DMBA) initiated and 12,0tetradecanoylphorbal -13-acetate (TPA) promoted skin tumors . The general anti-carcinognic effect of Curcumin involves the mechanisms like induction of apoptosis and inhibits cell-cycle progression, both of which are instrumental in preventing cancerous cell growth in rat aortic smooth muscle cells . The antiproliferative effect is mediated partly through inhibition of protein tyrosine kinase and c-myc mRNA expression and the apoptotic effect may partly be mediated through inhibition of protein tyrosine kinase, protein kinase C, c-myc mRNA expression and bcl-2 mRNA expression . Specifically, Curcumin suppresses human breast carcinoma through multiple pathways. Its antiproliferative effect is estrogendependent in ER (estrogen receptor)-positive MCF-7 cells and estrogenindependent in ER-negative MDA-MB-231 cells . Curcumin also down regulates matrix metalloproteinase (MMP)-2 and upregulates tissue inhibitor of metalloproteinase (TIMP)-1, two common effector molecules involved in cell invasion. It also induces apoptosis through P53-dependent Bax induction in human

breast cancer cells . Since major side effect of anticancer drugs is bone marrow depression, the present study has investigated the effect of chronic turmeric treatment on hematological parameters. There was no significant difference in hematological parameters among the different treatment groups and control group. Hence it was evident that no bone marrow depression with turmeric treatment was observed, which is a major side effect with cytotoxic chemotherapy. In conclusion, the turmeric acts effectively both orally and topically initiation stage of mammary cancer than in the promotion stage of mammary carcinoma. This stage specificity of turmeric's anticancer activity must be established by further investigations. Hypericum perforatum (St. John's wort) is a perennial flowering plant, preparations of which are popular as an anti-depressant and are also being promoted as an alternative cancer therapy. Even though some preliminary pre-clinical investigations have generated encouraging findings, there are no clinical studies to show that St. John's wort would change the natural history of any type of cancer. St. John's wort may reduce the blood levels of many conventional drugs, including some cancer medicines. Rare adverse effects include psychological symptoms, allergic reactions and visual disturbances. Anticancer effects The anti-depressive effects of St. John's wort seem to rely on the inhibition of the re-uptake of serotonin, noradrenalin, glutamate and dopamine in the central nervous system .

Other known mechanisms of action include the modulation of interleukin-6 activity and gamma-aminobutyric acid receptor binding and antioxidant effects . There is preliminary evidence from in-vitro studies to suggest that constituents of St. John's wort have anticancer effects[33-35] . A range of mechanisms have been proposed based on results of pre-clinical studies, e.g. cytotoxic, apoptosis-inducing and anti-angiogenic effects. St. John's wort extracts exhibit cytotoxic and apoptosisinducing effects in neoplastic cell lines . They thus inhibit the growth of leukaemia and glioblastoma prostate cancer cells in vitro . Ex-vivo experiments have demonstrated anti-angiogenic activity effects . which theoretically could contribute to anticancer These effects may not be linked purely to hypericin but also to other ingredients of St. John's wort . Animal experiments have shown that St. John's wort inhibits pro-inflammatory cytokines . Hypericin also 19 18 has phototoxic effects, and St. John's

wort could thus have potential as a photodynamic agent for some types of skin cancer Collectively the evidence indicates that the threshold for phototoxicity of hypericin 20 is between 100 and 1000 ng/ml . Since serum and skin concentrations of hypericin after oral1 administration of recommended doses are below 100 ng/ml, photosensitivity is unlikely . Nevertheless, it was reported that 3 µM of activated hypericin induced a necrotic mode of cell death in pigmented melanoma cells and melanocytes and an apoptotic mode of cell death in non-pigmented cells and keratinocytes .

Cancer is a multi-mechanistic second largest disease in the world require a multidimensional approach for its treatment, control and prevention. Plant based drugs form an important component of total medicines available for treating various human diseases. The use of phytochemicals in cancer prevention has received considerable interest in the past few decades owing to certain discoveries with specific properties include antioxidant and anti-inflammation. Recently, a number of anti-cancer agents have become recognized therapies in the clinical setting which include: vinca alkaloids, taxanes, podophyllotoxin, camptothecin and its derivatives . A number of additional plantderived agents are currently under investigation for example Homoharringtonine, 4-Ipomeanol and ß-lapachone .

Among the Acacia species, especially A.nilotica, a plant with established medicinal properties was chosen for this study. It has been reported as important medicinal plant used in folk medicine to treat various ailments. Based on this information and previous biological studies, we decided to investigate its anticancer effect against DAL induced solid and ascitic tumor condition. The reliable criteria for judging the quality of any anticancer drug are prolongation of lifespan and its effect on hematopoietic system . Administration of A.nilotica extract at concentration of 10 mg/kg.bw showed increase in mean survival time and percentage increase in life span, decrease in percentage of increase in body weight (due to reduction of tumor burden) when compare to control DAL bearing ascitic tumor group. Myelosuppression and anemia have been frequently observed in ascites carcinoma condition. and similar findings were observed in our present study. In DAL bearing

tumor control animals, elevated total WBC count and reduced hemoglobin content was observed. Moreover, A.nilotica extract showed a protective effect on hematopoietic system by reversal of total WBC cells and hemoglobin content in DAL bearing animals towards the value of normal group animals when compare to DAL bearing ascitic tumor animals. To investigate the inhibitory effect on ascitic tumor was local or systemic, the effect of administration of A.nilotica extract was tested against solid tumor induced by DAL cell lines. The abnormal mass of tissue that does not contain cyst or liquid is referred as solid tumor and is mostly epithelial in nature . We observed significant inhibition of solid tumor volume and reduction of body weight in solid tumor bearing animals when compare to control DAL induced solid tumor animals undoubtly suggests that the inhibitory effect of A.nilotica is systemic, not only related to its local cytotoxic effect.

This inhibitory effect on tumor volume and protection of hematopoietic system was comparable with the result produced by the standard drug methotrexate. AST and ALT were found in serum and various body tissues but are mostly associated with liver parenchymal cells. The elevated level of AST and ALT will be observed in acute liver damage condition. In addition, the level of ALP will rise with intrahepatic cholestasis and infiltrative diseases of the liver . Similarly in our present study, we observed elevated level of AST, ALT and ALP in DAL induced ascitic tumor animals when compare to DAL induced tumor alone group. Administration of A.nilotica extract and standard drug methotrexate exerted a protective effect by reversal of these enzyme levels nearly towards normal value of animals. Gamma glutamyl transferase, an enzyme involved in cellular glutathione homeostasis which is often increased in level in tumor condition. The membrane bound enzyme GGT is expressed highly in embryo livers and decreases rapidly to lowest levels after birth. GGT is highly re-expressed during the development of (HCC) Hepatocellular carcinoma . Treatment with A.nilotica significantly lowered the enhanced level of γ- GT in tumor bearing animals when compare to tumor control. The major non-protein thiol, GSH is required for the tumor cell proliferation and its metabolism . Cancer cells have higher GSH levels than the surrounding normal cells, which is characteristic of higher cell proliferation rate and resistance to chemotherapy. Scientific evidence shown that

combining GSH depletion using 1,3- Bis(2chloroethyl)-1-nitrosourea chemotherapy with superoxide dismutase gene therapy could be considerably successful in the treatment of breast cancer. When the intracellular GSH levels are low, the cells are more susceptible to ROS attacks. Increased ROS might activate different intracellular oncogenic pathways which lead to activation of tumorigenesis process. However, the excessive levels of ROS stress can also be toxic to the cancer cells. Therefore, changing ROS levels by GSH modulation is a way to selectively kill cancer cells without causing toxicity to normal cells. Administration of A.nilotica extract significantly reduced the level of intracellular GSH in extract treated DAL tumor cells when compare to the non-extract treated DAL bearing animals. Moreover, the treatment with extract also reduce the level of Nitric oxide production in serum and tumor cells when compare with tumor control animals.

Since, nitric oxide is an important regulator of tumor growth and involved in various pathophysiological process includes inflammation and carcinogenesis . Phenolics and flavonoids display a wide range of biological and pharmacological properties and normally scavenge the free radicals and play an essential role in prevention and therapy of cancer. It is well documented that A.nilotica is one of the rich source of these flavonoids and phenolics. For example, the polyphenolic compound Kaempferol displayed radical scavenging activity in different in vitro assays . Niloticane isolated from the bark of the A.nilotica showed antiinflammatory property by inhibition of Cyclooxygenase enzymes which is involved in inflammatory process . ß-sitosterol also showed antioxidant and anti-inflammatory activity, which is used in the treatment of inflammatory disorders, breast cancer and colon cancer (Padmasri and Sarada, 2011).

Similarly, gallic acid and catechin showed protective effect against N-nitrosodiethylamine-induced hepatocarcinogenesis (Brahma et al., 2009). Umbelliferone is also reported as potential scavenger of free radicals which is present in bark and leaves of A.nilotica. Recently, a report indicates that apigenin can act as potential chemopreventing agent due to induction of leukemia cell cycle arrest. Apigenin inhibited phosphoinositide 3- kinase/protein kinase B (PI3K/ PKB) pathway

in HL60 and induced caspase-dependent apoptosis. Androstene also exhibits dose dependent antiinflammatory property against TPA (12-Otetradecanoylphorbol-13-acetate) induced mouse ear edema .The anti-angiogenic effect of rutin and its regulatory effect on the production if VEGF, IL-1β and TNF-α in tumor associated macrophages was also demonstrated). the treatment with A.nilotica was effective on inhibiting the tumor progression *invivo* models, most likely because of high content and synergistic activity of specific constituents present in the extract such as umbelliferone, gallic acid, niloticane, catechin, kaempferol, rutin, apigenin, androstene and β-sitoterol derivatives may exert these preventing effects. However, the exact molecular mechanism by which A.nilotica mediates its antitumor activity is still not clear. Recently, there has been renewed interest in botanically derived products as sources of therapeutic agents, due to safety concerns with synthetic drugs. Lack of characterization of agents with specific actions, especially in supplements from natural products; have made clinicians and scientists wary of their efficacy. In the present study we report on the anticancer activity of the methanolic extract of the bark of Acacia catechu.

The plant from the family leguminosea is popular in Indian subcontinent as well as in various other Asian countries for 'katha 'preparation. Katha is extracted from the hardwood and bark of Acacia catechu. However as per our findings the bark appears to be of great importance. The anticancer activity of Acacia catechu was evaluated in different cell lines viz. KB, MCF-7, U-87, HeLa, NCLH46, and HEK. Different extracts of the bark were tested for cytotoxic activity. Among all the extracts tested, the methanolic extract caused significant inhibition in the growth of cancerous cells. It caused inhibition of growth of KB cell line by ~83% . methanolic extract was much slower in comparison to the untreated cells. Even at the end of 12 hours the cells were not able to fill up the artificial gap upon treatment while the gap was filled successfully by untreated cells. The above study proved the fact that the plant extract has the potential to slow down the process of metastasis. Along with the cell migration assay, morphological changes in the cells during treatment with the methanolic extract were also studied. The cells were observed after every 6 hours under phase contrast microscope. Cells were found to lose their adherent ability and

shrinkage in cells was observed upon treatment with methanolic extract. The cells loose their adherent projections and come on the surface and become aggregated which finally leads to their death. A vast variety of naturally occurring substances have been shown protection against experimental carcinogenesis. Some antiinflammatory chemopreventive agents have been found to suppress growth and proliferation of transformed or malignant cells through apoptotic induction. Our results demonstrated that methanolic extract from Acacia catechu induced apaptosis in KB cells at concentrations of 100 µg/ml and 200 µg/ml, as demonstrated by DNA fragmentation assay. The induction of apoptotic cell death was also accompanied by characteristic morphological and structural changes. The western blot analysis clearly illustrates the inhibitory effect of the methanolic extract on Cyclooxygenase-2 enzyme (COX-2) level activity. The expression of the COX-2 protein is lowered to a significant extent upto 75% in oral cancer cells, which were treated with the methanolic extract as compared to those cells which were untreated. COX-2 is related to the formation of carcinogens, tumor promotion, apoptosis inhibition, angiogenesis development, and metastatic process.

The inhibition in metastatic potential and cytotoxicity in oral cancer cells could be correlated to COX-2 inhibition. We propose here that the methanolic extract of the bark of Acacia catechu not only has cytotoxic action on cancerous cells, but also prevents metastasis. The study also revealed the fact that the extract leads to apoptosis in the cancerous cells as indicated by DNA fragmentation and inhibition in the COX-2 enzyme activity. Therefore the methanolic extract causes cells to aggregate, decrease proliferation and to enter apoptosis. Several mechanisms involved in GTCs inhibition of cancer formation/progression are recently reviewed by numerous Authors . Certainly, GTCs, through their antioxidant activity, are able to quench ROS and chelate transition metals, produced during all the carcinogenesis stage. However, it has been reported that also GTCs can be a source of ROS generation, inducing oxidative stress and consequently activating apoptotic pathways . GTCs, and especially EGCG, are capable of modulating a plethora of cell signalling pathways crucial for cancer cells transformation and survival, including, but not limited to, the mitogen-activated protein kinase (MAP-kinase), the nuclearfactor-kappaB(NFκB),

and the insulin-like growth factor (IGF)/IGF-1 receptor pathways. With regard to the prostate-specic processes GTCs are able to affect androgen receptor (AR) downregulation and prostate-specic antigen (PSA) expression . Here below, we report the most probable GTCs mechanisms of action in some PCa cell lines. 2.1. Inhibition of Cell Proliferation and Cell Cycle Arrest. GTCs exhibit ant-proliferative effects versus both androgensensitive and androgen-insensitive human PCa cells. The effect is mediated by cell cycle deregulation and cell death induction. We showed that GTCs action is cancer specic, since GTCs is capable of inducing growth arrest both in SV40 immortalized prostate epithelial cells (PNT1a) and in tumorigenic androgen-independent PCa cells (PC3), while normal human prostate epithelial cells were not signicantly affected, even when EGCG was administered at higher doses. The IC50 of EGCG ranges from about 40 to about 200μM, depending on the cell line type (LNCap < PNT1a < DU145 < PC3), as well as the length of the experiment, ranging from 24 to 72 hours .

Our results were conrmed by other authors in normal broblasts Antioxidant activities of GSE and grape phenolic compounds (mainly resveratrol and procyanidins), have been extensively investigated in vitro and in vivo.GSE possesses strong free radical scavenging activity prevents ROS-induced DNA damage and displays a relevant chelating effect on transition metal ions, thus reducing lipid peroxidation . Those effects have been deemed even more potent than known antioxidants such as vitamin E and ascorbic acid. Some studies have reported an enhancing effect of GSE or of its polyphenolic constituents, on several anti-oxidant enzymes as glutathione (GSH) super-oxide dismutase (SOD) catalase and other detoxifying/antioxidant enzymes . GSE-induced antioxidant enzyme expression is associated with activation of the redox-sensitive transcription factor nuclear factor erythroid-2 p45 (NF-E2)-related factor (Nrf2), through its interaction with the antioxidant-response element (ARE) or the electrophile-responsive element (EpRE) . Indeed, Nrf2 plays a key role in up-regulation of many phase II antioxidant/detoxifying enzymes, including glutathione peroxidase (GPx), glutamate cysteine ligase (GCL), glutathione S-transferase (GST), SOD, and NADPH/quinone oxidoreductase 1 (NQO1) .In vivo, dietary supplementation of GSE was shown to reduce oxidative stress and improve the

glutathione/oxidized glutathione ratio, as well as the total antioxidant in a double-blinded randomized crossover human trial .Though those results have been often confirmed , other studies have been unable to do so, showing that GSE exhibits either only a moderate or negligible antioxidant effect .

Oxidative stress, resulting from enhanced production of ROS overcoming the cellular antioxidant defence, is a key phenomenon in chronic degenerative diseases (diabetes mellilitus, cardiovascular illness, cancer) ROS participate in triggering the apoptotic process, as programmed cell death is tightly regulated by the oxidative environment . Dietary GSE strongly reduces rat mucosal apoptosis via modulation of both mitochondrial and cytosolic antioxidant enzyme systems together with an increase in cellular GSH, thus protecting normal colonic mucosa from ROS injury . Given that GSE exerts a protective antioxidant effect in normal cells exhibiting deficiency of catalase activity or glutathione level, it can be hypothesized that grape polyphenols participate in controlling intracellular peroxide production .

Hence, anti-oxidant properties of GSE treatment may efficiently counteract the onset of ROSdependent disease, as documented by several studies. Yet, despite the popular version diffused by mass-media, it is hardly conceivable that GSE or polyphenols may exert a significant effect against cancer development by displaying anti-oxidant actions . Indeed, several studies have reported that GSE in cancer cells paradoxically enhances ROS production in a significant manner. GSE and many polyphenolic compounds induce a relevant increase in ROS and in superoxide radical generation, at both the cytosolic and mitochondrial site, that could eventually lead to GSH depletion . It is worth noting that GSE does not induce hydroxy peroxide (H2O2) increase, thus evidencing a deficiency in SOD activity, at least in the cancer cell lines studied. Indeed, in SODdeficient cells, GSE treatment induce ROS-mediated cytotoxicity, evidencing that GSE-dependent increase in ROS activity is not efficiently counteracted by SODdependent transformation in hydroxy peroxide, leading to GSH depletion, cellular damage, and increased apoptosis Moreover, pro-oxidant effects of GSE are enhanced in cells lacking SOD activity meanwhile coexposures of polyphenols-treated cancer cells with SOD largely prevented ROS formation and

DNA damage Considering that the oxidant-dependent toxicity of polyphenols is efficiently rescued by co-treatment with SOD, but not with catalase, it is unlikely that flavonoidsrelated pro-oxidant effects could be mediated.

Cancer continues to be and is increasingly a serious health problem and one of the leading causes of death in the world. Aging and the growth of the world population changes in life style and the adoption of cancer causing behavior are some of the reason for this prevalence. According to cancer statistics in 2013, stomach and liver cancer are the most common in Asia and both are associated with high mortality rates, while bladder cancer is the most common in USA. Colorectal and breast cancers have high incidence rates in all countries. Cancer has been a constant battle globally with a lot of development in cures and preventative therapies. The disease is characterized by cells in human body continually multiplying with the inability to be controlled or stopped. Consequently, forming tumors of malignant cells with the potential to be metastatic. Current treatments include chemotherapy, radiotherapy and chemically derived drugs. Treatments such as chemotherapy can put patient under a lot of strain and further damage their health. Therefore, there is a focus on using alternative treatments and therapies against cancer. For many years herbal medicines have been used and are still used in the developing countries as the primary source of medical treatment. Plants have been used in medicine for their natural antiseptic properties. Thus, research has developed into investigating the potential properties and uses of terrestrial plants extracts for the preparation of potential nanomaterial drugs for diseases including cancer. Many plant species are already being used to treat or prevent development of cancer. Multiple researchers have identified species of plants that have demonstrated anticancer properties with a lot of focus on those that have been used in herbal medicine in developing countries. Compounds which are characteristic to the plant kingdom and are necessary for the plant survival and "housekeeping" .

A disease originated by an uncontrolled splitting up of anomalous cells in a fraction of the body is called cancer. Cancer cells typically attack as well as obliterate normal cells. Cancer is one of the foremost public health burdens in both developed and

developing countries . In Bangladesh, 13% death due to disease belongs to cancer. Natural Products such as plants have been used for the treatment of different diseases for thousands of years. Global plants have been used as medicines in Egypt, China, India and Greece and in many countries from ancient time and an extraordinary number of modern drugs have been developed from them [4-9]. Medicinal plants remain on to be a central therapeutic assist used for alleviating ailments of human race. Over the last 2500 years, here have been very strongly built traditional systems of medicine such as Ayurvedic, and the Unani . These plants restrain materials that can be utilized for useful purposes, of which are originators for the synthesis of drugs. Plenty of research work has been carried out on a number of medicinal herbs as well as they have been initiate to have definite action on the respiratory, nervous, circulatory, digestive and urinary organisms, sexual organs, skin, hearing, vision, and taste. The exploration for anti-cancer means on or after plant sources started during the 1950s. Moreover like other countries in Bangladesh, there are lot of research has been done and some research is still going on as it is to be mentioned that till now the best source of anticancer agents is medicinal plant . The major target of this review article was to give some information to Bangladeshi researchers about some medicinal plants having anticancer properties available in Bangladesh.

Allium sativum (Allicin) Allium sativum (garlic, lasun) is worn to treat a wide diversity of diseases in Bangladesh. It is cultivated in most of the districts of Bangladesh . Allicin is a principal constituent of raw garlic . Some research demonstrated that its cytotoxic effect has been experienced using a everlasting, human principal fibroblasts, non tumorgenic cell line significant from baby hamster kidney cells and a tumorgenic lymphoid cell line ensuing from a Burkitt lymphoma . It was also instituted that the cytotoxic exploit was in the range 2-50μg/ml. It is to be mentioned that the most important fact is a number of organo-sulfur compounds commencing garlic, like S-allylcysteine, are accounted to inhibit the growth of chemically persuaded besides transplantable tumors in reasonably a lot of animal models. Achyranthes aspera Achyranthes asperaLinn is an often originated herb as an uncultivated plant on road sides all through Bangladesh . It is derived from all over the country in way sides along with crop-free lands . The methanol extract of its alkaloid along with non-alkaloid and

saponin fractions have been verified noteworthy inhibitory belongings on the Epstein-Barr virus close to the starting antigen commencement persuaded by the carcinogen 12-O-tetradecanoylphorbol-13-acetate in Raji cells at a concentration of 100µg. Throughout in vivo it is found that twostage mouse skin carcinogenesis examination the total methanol extract obsessive a pronounced cytotoxic tumult and in vitro study it is found that the non-alkaloid portions containing mainly non polar complexes showed the bulk of note inhibitory act . Andrographis paniculata It is originated in Chittagong and Chittagong Hill Tracts . A number of previous phytochemical study of the ethanol extract of the airborne fractions of Andographis paniculata has been noted the segregation of 14 compounds as well as a better part of them are labdane diterpenoids and also flavonoids . It is to be mentioned that the cytotoxic actions of these compounds have been reviewed against a variety of cell lines and instituted with the rationale of these isolates have a strong tumour inhibitory activity bordering to all examined cell lines which is very considerable. Also, there are a few unnecessary side effects were additionally reported which may embrace gastric upset and fatigue, headache and disturbance of the regular functions of liver and bitter taste too . Cannabis sativa It is originated in Dhaka, Chittagong, Chittagong Hill Tracts, Dinajpur, Faridpur, Jessore, Kushtia, Rajshahi, Rangpur . The dynamic mechanisms of Cannabis sativa are known as cannabinoids. Some previous research demonstrated that in vitro studies of apparatus of marijuana (Cannabis sativa) assign a prospective to reduce human breast cancer cells and also to build tumor eradications. It is also significant to know that in some experiments bringing in marijuana to malignant brain tumors, it was recognized that continued survival of animals was increased Camellia sinensis (Green Tea) It is basically found in Sylhet, Moulvi Bazar, Chittagong, Chittagong Hill Tracts, Panchagar and Dinajpur . It is to be mentioned that the majority abundant polyphenol in green tea is Epigallocatechin-3-gallate (EGCG). Some previous research demonstrated that EGCG suppress the growth of cancer cell lines similar to hepatocellular carcinoma from side to side beginning of cell cycle arrest. Moreover, some research showed that the increase of cancer cells within ovarian carcinoma is as well inhibited cell EGCG . Oroxylum indicum It is originated in the forests of Chittagong, Cox's Bazar, Chittagong Hill Tracts, Dhaka-Tangail and also in village shrubberies and farmhouses all through the

country . The plant is used in a variety of polyherbal formulations Bangladeshi method of medicine. Some previous studies have established anticancer potential of Oroxylum indicum by means of a range of models furthermore stated in some research that 95% ethanol extract illustrated cytotoxic activity contiguous to Hep2 cell lines at a manifestation of 0.05% and most importantly extract of Oroxylum indicum established the toxicity on tumor cell lines tested while aqueous extracts and methanolic of Oroxylum indicum have been demonstrated prevalent cytotoxicity in chosen tested cell lines . Terminalia chebula Terminalia chebula is found in Dhaka, Chittagong, Tangail; cultivated in many parts of the country . The plant is a superior source of hydrolysable tannis and also its anti mutagenic feat in Salmonella typhimurium has been recognized in some research. Some prior research stated that Terminalia chebula fruits crush along with its acetone haul beyond bark have been accounted with capable of anti mutagenic and anti carcinogenic association in addition to most importantly Phenols akin to chebulinic acid and ellagic acid and tannic acid are the cancer growth inhibitors introduced within the fruits of Terminalia chebula . Withania somnifera (Withanolides) It is basically originated in North Bengal site of Bangladesh. Withania somnifera is extremely valued in Ayurveda intended for cancer patients. It is also used as a remedy for fighting the cancer like situation. It is to be mentioned that the roots of Withania somnifera are helpful parts. A number previous research remarked that during vitro study with anolides from Withania somnifera abridged the enlargement of cancer cells in human breast as well as central nervous system . Zingiber officinale It is cultured all over the country. Some research were done previously on Zingiber officinale and found that ethanol extract to find out its antitumor possessions in skin tumor genesis model of mice and also on top of the skin of mice resulted in essential reticence of 12-0-tetradecanoylphorbol-13-acetate (TPA) rational initiation of epidermal ODC and additionally cyclo oxygenase and lipoxygenase actions. Some research on natural bio-actives of entirely ginger extract and 6-gigerol suggested a mechanism of act of ginger extract on colon cancer cells perhaps striking the G0/G1- phase, reducing DNA synthesis and its oppression . Mangifera indica It is a very common fruit in Bangladeshi market. It is found and cultivated all over Bangladesh . It is a nutritional add-on used in frequent tribes as a folklore medication. Some prior research on Mangifera indica stated

that it showed a huge enhancement of excellence of life in cancer patients and that is the most significant fact about the plant . Curcuma longa L It is cultivated all over Bangladesh. It is found that turmeric has been used in the Chinese and Indian pharmacopoeia from ancient time. It is known that turmeric's active ingredient is an extracted compound called curcumin. Some previous studies showed that that curcumin helps to prevent several forms of cancer including lung, breast, stomach, liver, and colon because of its anti-inflammatory as well as antioxidant properties. It stops the growth of cancer by interfering with the cellular signaling phases of cancer . Syzygium aromaticum It is cultivated all over Bangladesh. The previous research showed that clove essential oil relates to its anti-cancer benefits. It has the ability to kill cancer cells and as a natural chemo preventive agent. Clove essential oil has been found to contain cytotoxic which means cancer cell killing properties against a line of breast cancer cells known as MCF-7 . Allium cepa It is cultivated in most of the districts of Bangladesh. Some previous study has found that a natural compound collected from onions named onion in A (ONA) has quite a few anti-ovarian cancer properties. The effects of ONA were texted on a preclinical model of epithelial ovarian cancer (EOC) both *in vivo* and *in vitro*. The outcome was satisfactory.

Plant derived agents are being used for the treatment of cancer. Several anticancer agents from plants include; taxol, vinblastine, vincristine, the camptothecin derivatives, topotecan and irinotecan, and etoposide derived from epipodo phyllotoxin are in clinical use all over the world. Numerous cancer research studies have been conducted using traditional medicinal plants in an effort to discover new therapeutic agents that lack the toxic side effects associated with current chemotherapeutic agents and the drugs under clinical phytomedicines has increased dramatically in the last two decades. It has been also reported that more than 50% of all modern drugs in clinical use are of natural products, many of which have been recognized to have the ability to include apoptosis in various cancer cells of human originals, there is an urgent need to develop much effective and less toxic drugs.

In vitro studies. Geinstien in plants such as parsley and soy foods inhibits protein try osine kinase, thereby disrupting signal transduction andinducingcell differentiation. Herbs dactylon. Pers. belongs to the family of Poaceae and is said to have many medicinal properties including Antihelmentic, Antidiuretic, petroleum eather Antiinflammatory, Hepatoprotective activity as well as treatment of Urinary tract infections , Prostatitis, and Dysentery. Traditionally it is used in diabetes jaundice, kidney problems, urinary disease, gastro intestinal disorder, Constipation and abdominal pain. The whole plant is used for diuretic, dropsy, syphilis, wound infection and piles. Herbsis used as antihemorrhagic in dysentery and nasal bleeding. The juice of the plant is astringent and is applied externally to fresh cuts and wounds. It is used in the treatment of catarrhal ophthalmia, hysteria, epilepsy, insanity, and chronic diarrhea. The plant is folk remedy for anasarca, calculus, carbuncles, cough, hyper tension, snake bites, gout and rheumatic affections.

Cancer is one of the most dreaded diseases of the 20th century and spreading further with continuance and increasing incidence in 21st century (Balachandran et al., 2005). Current scientific interest in the management of cancer is directed towards the utilization of naturally occurring compounds that possess anticancer properties. Since 1950, major efforts have been taken for the discovery of naturally occurring anticancer drugs (Cragg et al., 2005). In developing countries alone it is estimated about 80% of the population rely on traditional medicines for their primary health care because of their wide biological activities, higher safety margin and cost effectiveness (Palav et al., 2006). Microalgae are valuable sources of many unique biologically active compounds including anticancer compounds. Algae have become the focus, of extensive research efforts aimed at finding novel compounds that might lead to therapeutically useful agents. (Mendes et al., 2003; Cardozo et al., 2007). It is proposed that the development of effective chemotherapeutic strategies based on herbal medicine, aided with understanding their mode of action, should provide useful information for their application in cancer therapy and prevention. The study aims to understand the chemotherapeutic and various pharmacological roles of microalgae, Desmococcus olivaceus and Chlorococcum

humicola in attenuating the cancer. Such an understanding will promote further research and clinical trials using microalgae as a potent anticancer agent.

The burden of cancer rose to 18.1 million new cases and 9.6 million deaths in 2018. With 36 different types, cancer mainly men in the form of colorectal, liver, lung, prostate, and stomach cancer and women in the form of breast, cervix, colorectal, lung, and thyroid cancer. Treating cancer has become a whole new area of research. There are conventional as well as very modern techniques applied against cancers. A variety of techniques i.e., chemotherapy, radiation therapy, or surgery are used for treating cancer. However, all of them have some disadvantages. The use of conventional chemicals bears side effects and toxicities. But as the problem persists, new approaches are needed for the control of diseases, especially, because of the failure of conventional chemotherapeutic approaches. Therefore, there is a need for new strategies for the prevention and cure of cancer to control the death rate because of this disease.

Herbal medicine has become a very safe, non-toxic, and easily available source of cancer-treating compounds. Herbs are believed to neutralize the effects of diseases in a body because of various characteristics they possess. For instance, among the many anticancer medicinal plants,

Phaleria macrocarpa (local name: Mahkota dewa) and Fagonia indica (local name: Dhamasa) have been used traditionally for the anticancer properties of their active ingredients. Metabolites extracted from the plant material are used to induce apoptosis in cancer cells. Gallic acid as the active component was purified from the fruit extract of P. macrocarpa and has demonstrated a role in the induction of apoptosis in lung cancer, leukemia, and colon adenocarcinoma cell lines. It is a polyhydroxy phenolic compound and a natural antioxidant that can be obtained from a variety of natural products i.e., grapes, strawberries, bananas, green tea, and vegetables. It also plays a critical role in preventing malignancy transformation and the development of cancer. Similarly, other compounds such as vinca alkaloids, podophyllotoxin, and camptothecin obtained from various plants are used for the treatment of cancer.

With the advancement in the industrial sector and industrial medicine, the use of herbs was forgotten for a long period of time. Hurdles regarding natural compounds are reduced because of the advent of new techniques and interest has been developed in the

use of such natural ingredients in the pharmaceutical industry. It has been estimated by the world health organization that 80% of the world is using traditional treatment methods. Understanding of the effects or actions of herbs on various targets comes with the help of modern biomolecular science which recognizes some important properties i.e., anticancer, anti-inflammatory, and anti-virus. With the increasing understanding of the effects of such herbal medicine, their effects against different types of cancers have also been identified. For instance, hepatocellular carcinomas (HCC) are considered as the fifth most common malignancy in the world with increasing incidence. Many studies have been performed on the treatment and prevention of using herbal medicine against HCC in which it is shown that all phases of HCC such as initiation, promotion, and progression could be affected by components of herbs. However, as far as herbal compounds are considered as drugs, it is erroneously believed that they have no issues in terms of safety and side effects. There are hundreds of species of plants that are toxic to health. In the same way, there are many compounds in otherwise friendly plants that cause cytotoxicity. Based upon testing it has been proved that even anticancer plants result in cytotoxic effects.

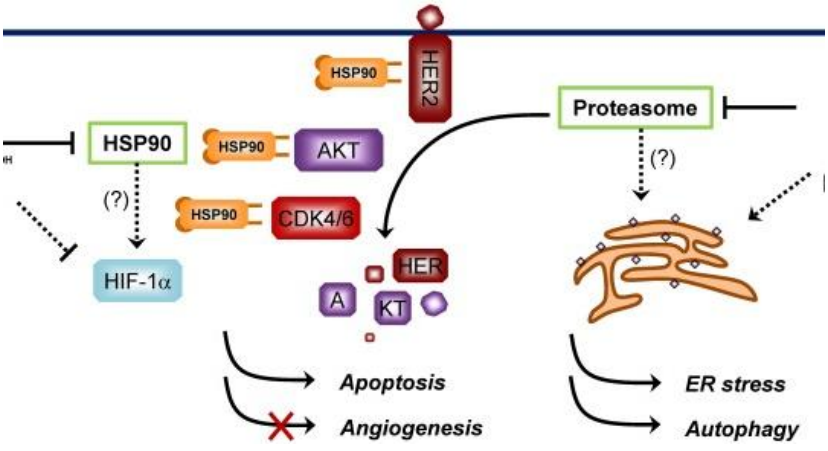
Herbs are regulated under the "dietary supplement health and education act" as a dietary supplement in the United States of America. This review highlights the mechanism of some very important anticancer plants, the research related to their mechanism of action, their active ingredients, and the guidelines in place for their regulations.

The development of cancer registries throughout the world has led to a search for novel drugs that are toxic to the cancer cells while having no harmful effect on normal cells. The anticancer drugs used previously exhibited relatively high toxicity not only to the tumor cells, but also to the normal cells of the body part in which the cancer had developed. Currently, the search for novel anticancer drugs is being conducted among terrestrial plants, as well as in marine environments. Plants have been used for centuries to treat diseases. In various parts of the world, several plants are consumed for their health benefits as a part of traditional folk medicine. The increase in the incidence of various types of cancer creates a need for new anticancer drugs. For example, in 2017, 1,688,780 new cancer cases and 600,920 cancer deaths are projected to occur in the United States. Numerous anticancer drugs isolated from plant materials are tested on cells

(including various cancer cell lines) and experimental animals after purification and then sent to clinical trials. In recent years, there has been a dynamic increase in the number of newly discovered natural compounds. In 2006, about 50,000 such substances were known, whereas, in 2014, the number of the newly discovered molecules increased to approximately 326,000. Among these, there were approximately 170,000 compounds in the toxicity class. In addition, there are 195,000 pharmacologically active compounds for which the interactions are quantitatively known. Plants that have been used in traditional medicine for centuries have found application as sources of materials that possess high biological activity. One approach is to obtain these substances through extractions from the plant materials. Another approach is to use biotechnological tools to produce plant-derived anticancer compounds. The substances of natural origin (e.g., from plants and aquatic animals) that exhibit antitumor properties belong to various groups of compounds, such as alkaloids, diterpenes, diterpenoquinone, purine-based compounds, lactonic sesquiterpene, peptides,

cyclic depsipeptide, proteins, macrocyclic polyethers, etc. Sometimes, the cost of extraction.

Figure. No: 1: The Mechanism of Anticancer activity



Herbsis a valuable herbal medicine and used for first aid for minor injuries. Herbsis bitter, sharp hot taste, good odor, laxative, brain and heart tonic, aphrodisiac, expectorant, carminative and useful against grippe in children and for pains, inflammations and tooth

ache. Virus-affected discolored leaves of Herbs are used for the treatment of liver complaints. In Homoeopathic systems of medicine, it is used to treat all types of bleeding and skin troubles. The petroleum ether extract of aerial parts of C. dactylon showed marked protection against convulsions induced by chemo convulsive agents in mice. Petroleum ether extract of defatted C. dactylon has high antidiabetic potential along with good hypo lipidemic profile. This suggests the potential for Herbs to become an alternative to current diabetes medications. The methanolic extract of Herbs possessed significant

1.1 Lung cancer,

Lung disease otherwise called dangerous lung tumor described by uncontrolled cell development in tissues of the lung. Most malignancies that begin in the lung, known as essential lung tumors, are called as carcinomas. The two fundamental sorts are little cell & non-little cell. The most widely recognized side effects are hacking, weight reduction, shortness of breath, & trunk torments. Most by far (85%) of instances of lung superfluous augmentation expansions are because of long haul tobacco & smoking. Around 10–15% of cases happen in individuals who have never smoked. These cases are regularly created by a blend of hereditary elements & air contamination. Lung disease might be seen on trunk radiographs & processed checks. The finding is affirmed by biopsy which is typically performed.

Counteractive action is by dodging hazard elements including smoking & air contamination. Treatment & long haul results rely on upon level of diseases, the level of spread & the people general wellbeing. Mostcases are not reparable. Basic medications incorporate surgery, chemotherapy, & radiotherapy.

1.1.1 Signs & side effects of lung tumor.

The ADRs announced, for example, hacking, wheezing, weight reduction, shortcoming, fever, trunk torment, bone agony, prevalent vena cava deterrent, breathing troubles, pneumonia & hypocalcaemia.

1.1.2 Analysis

Playing out a trunk radiograph is the initial step to analyze lung tumor. This may uncover an undeniable mass, extending of mediastinum, atelectasis, & pneumonia. CT imaging is normally utilized to give more data about sort & degree of disease. Guided regularly utilized to be test for tumor histopathology. Disease regularly shows up lone aspiratory knob on a trunk radiograph.

1.1.3 Clinical practice rules

Prescribe frequencies for pneumonic knob observation. CT imaging ought not be utilized for more / more oftentimes than showed stretched out observation opens individuals to be expanded radiation.

1.1.4 Order of lung

Lung diseases are arranged by histological sort. . Lung growths are carcinomas that emerge from epithelial cells. For remedial purposes, two wide classes are recognized as non-little cell & little cell lung carcinoma[1-8].

1.1.5 Non-little cell lung carcinoma

The three principle subtypes of NSCLC are adenocarcinoma, squamous-cell carcinoma & huge cell carcinoma. Almost 40% tumors have been adenocarcinoma ordinarily begins fringe lung tissue. Albeit most instances related amid smoking has additionally most well-known type lung disease among individuals who have smoked. Subtype bronchioloalveolar carcinoma more basic in female never smokers & might have superior long haul survival. Squamous cell represents around 30% of lung malignancies. They commonly happen near vast aviation routes. An empty pit & related cell passing are normally found at the focal point of the tumor. Around 9% diseases were expansive cell .

1.1.6 Little cell lung carcinoma

In SCLC contain thick granules, which give this tumor an endocrine disorder. Sixty to seventy percent have broad illness (which can't be focused inside a solitary radiation treatment field) at introduction.

1.1.7 Treatment for Lung growth

Momentum inquire about guidelines for lung treatment incorporate immunotherapy, which energizes the body's resistant framework to assault the tumor cells, epigenetic, new mixes of chemotherapy & radiotherapy. A number of these new medicines work through invulnerable checkpoint bar, upsetting disease's capacity to sidestep the resistant framework. Other immunotherapy medicines meddle amid the official of modified cell passing protein amid its ligand PD-1 ligand 1. Motioning through PD-1 inactivates T cells. Some growth cells seem to adventure this by communicating PD-L1 amid a specific end goal to turn off T cells that may remember them as a danger. Monoclonal antibodies

focusing on both PD-1 & PD-L1, for example, pembrolizumab & nivolumab are right now in clinical trials for treatment for lung growth. Epigenetics is the investigation of little, heritable, atomic alterations that dilemma DNA & adjust quality expression levels. Focusing on these labels amid medications can execute tumor cells. Early-organize examine in NSCLC utilizing drugs went for epigenetic adjustments demonstrates that blocking more than one of these labels can murder cells amid less symptoms. Ponders additionally demonstrate that givingindividualsthese medications before standard treatment can enhance its adequacy. Clinical trials are in progress to assess how well these medications slaughter lung cells in people. A few medications that objective epigenetic systems are being developed. Histone deacetylase inhibitors being developed. DNA methyltransferase inhibitors being developed incorporate decitabine, azacytidine, & hydralazine. For lung cases that create imperviousness to epidermal development consider receptor & anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitors, new medications are being developed. New EGFR inhibitors incorporate afatinib & dacomitinib. An option flagging pathway, c-Met, can be restrained by tivantinib & on artuzumab. New ALK inhibitors incorporate crizotinib & ceritinib[9].

1.1.8 Screening

Tumor screening utilizes therapeutic tests to recognize illness in huge gatherings of individuals who have no manifestations. Registered screening can identify growth & give a man alternative to react to it in a way that delays life. This type of screening diminishes the possibility of death from lung growth by a flat out measure of 0.3%.

1.1.9 Avoidance methodologies

Treatment for lung disease relies on upon the growth's particular cell sort, how far it has spread, & the individual's execution status. Regular medicines incorporate palliative care surgery, chemotherapy, & radiation treatment. Focused on treatment of lung growth is developing in significance for cutting edge lung tumor.

1.1.10 Pancreatic tumor

Pancreatic tumor emerges in the pancreas start to duplicate & can attack different parts of the body. Signs & side effects incorporate yellow skin, stomach torment, weight reduction & loss of craving. Pancreatic growth happens before the age of 40 & the greater part of instances of pancreatic happen in those more than 70. Hazard elements for pancreatic tumor incorporate tobacco smoking, corpulence, diabetes & hereditary conditions. Pancreatic growth is normally analyzed by a mix of medicinal imaging methods, for example, ultrasound blood tests[10-14].

1.1.11 Exocrine tumor

Exocrine tumor is the most widely recognized kind of every single pancreatic growth. Almost all these begin in the pipes of the pancreas, & pancreatic ductal adenocarcinoma. This is in spite of the way that the tissue from which it emerges the pancreatic ductal epithelium – speaks to fewer than 10% of the pancreas by cell volume. Begins channels formation were convey emissions, for example, compounds & bicarbonate far from pancreas. Acinar carcinoma of the cell in the carcinoma emerges in the bunch of cells that create 5% of exocrine pancreas exaggerated. These growths are thought to emerge from a few sorts of precancerous injuries inside the pancreas in which pancreatic intraepithelial neoplasma are infinitesimal anomalies in the pancreas. Furthermore, intraductal papillary mucinous neoplasms are plainly visible sores, which happen in about of grown-ups, & danger of forming into tumor.

1.1.12 Neuroendocrine disease

The little minority of tumors that emerge in the pancreas are called as neuroendocrine tumors are a gathering of harmful tumors that emerge from the body's neuroendocrine cells, which are in charge of coordinating the apprehensive & endocrine frameworks. Indications which incorporates Pain in the upper guts, Jaundice,loss of hunger, sickness, stoppage & diabetes.

1.1.13 Chance components for pancreatic adenocarcinoma

Age & sexual orientation are the danger of creating pancreatic growth. Most cases happen after age 65 while cases before age 40 are unprecedented. The illness is marginally more regular in men than ladies. Cigarette smoking is the avoidable hazard figure for pancreatic tumor. Corpulence; a BMI more prominent than 35 builds the hazard by about half. Family history of 5–10% has pancreatic growth cases have an acquired part, where individuals have a family history of pancreatic superfluous intensification. Drinking liquor too much is a noteworthy reason for pancreatic cancer.[36]

Prostate tumor otherwise called the improvement of superfluous intensification in the prostate organ in male conceptive framework. Superfluous intensification cells may spread from the prostate to different parts of the body, especially through the bones & lymph nodes.Symptoms incorporate continuous pee, nocturia, trouble beginning & keeping up a constant flow of pee, hematuria, bonepain & dysuria. Prostate tumor is related amid urinary brokenness as the prostate organ encompasses the prostatic urethra. Changes inside the organ specifically influence urinary capacity**.**

1.1.14 Prostatic hyperplasia

An infection known as considerate prostatic hyperplasia may deliver comparable indications. Other late side effects may incorporate feeling tired because of low levels of red blood cells.

1.1.15 Signs & manifestations

The manifestations of laryngSBC superfluous intensification rely on upon the size & area of the tumor. Manifestations which incorporates voice changes, lump in neck, Persistent cough,Earache & trouble in swallowing.Treatment impacts can incorporate post-agent changes in appearance, trouble eating, or loss of voice. Analysis is made by the specialist on the premise of a medicinal history, physical examination, & unique examinations which incorporate a trunk x-beam, CT, MRI check, tissue biopsy, surgery, radiotherahy & chemotherapy.

1.1.16 Liver cancer

Threatening or destructive cells that create in the ordinary cells of the hepatocytes are called hepatocellular carcinoma. A superfluous intensification that emerges in the channels of the liver is called cholangiocarcinoma. Metastatic superfluous intensification in the liver is a condition in which disease from different organs has spread through the circulation system to liver. The liver has turned into the site to which the tumor that began somewhere else has spread. Their metastasis is found by X-beams. Growth of the liver or jaundice can demonstrate superfluous intensification has spread to the liver. The reasons for liver disease might be connected to ecological, dietary, or way of life variables.

1.1.17Colorectal disease

Colorectal disease is the tumor of the colon & rectum. A colorectal growth is harmful. Favorable means the tumor won't spread, while a threatening tumor comprises of cells that can spread to different parts of the body & harm them. Side effects incorporate Diarrhea, Constipation, and Blood in dung, & Pain in stomach area, Vomiting, Fatigue & weight reduction.

1.1.18 Treatment

The expulsion of cells or tissues frame human body, they can be seen under a magnifying lens to check for indications of disease. Tumor tissue that is expelled amid the biopsy might be verified whether the patient is probably going to have the quality transformation that causes treatment. The immune response is typically connected to a radioactive substance or a color that causes the tissue to illuminate under a magnifying instrument. This kind of test might be utilized to differentiate between various sorts of growth.

1.2 Carcinoembryonic antigen examine

The test are measures the level of CEA in the blood. CEA is discharged into the circulation system from both tumor cells & ordinary cells. At the point when found in higher than ordinary sums, it can be an indication of rectal growth or other conditions.Colonoscopy is a system to glimpse inside the rectum & colon for polyps, irregular regions, or superfluous intensification.

1.2.1 Kaposis sarcoma

Kaposi sarcoma is a tumor brought on by disease amid human herpesvirus 8 (HHV8), otherwise called Kaposi sarcoma-related herpesvirus (KSHV) or KS operator. It was initially depicted by Moritz Kaposi.Kaposi sarcoma (KS) is a systemic malady that can give cutaneous injuries amid or without inward inclusion.

1.2.2 Treatment

Once the analysis of KS has been made, treatment depends on the subtype & the nearness of limited versus systemic illness. Limited cutaneous ailment can be treated amid cryotherapy, intralesional infusions of vinblastine, alitretinoin gel, radiotherapy, topical immunotherapy (Imiquimod), or surgical extraction. Broad cutaneous malady as well as inner illness may require intravenous chemotherapy & immunotherapy.

1.2.3 Rhabdomyosarcoma

Rhabdomyosarcoma is a compelling & uncommonly risky sort of tumor that makes from skeletal (striated) muscle cells that have fail to totally isolated. It is generally thought to be a disease of youth, as by a long shot a large portion of cases occur in those underneath the age of 18. It is by & large delineated as one of the "little, round, blue cell tumors of youthfulness as a result of its appearance on an H&E recolor. Despite being a for the most part remarkable harm, it speaks to about 40% of all recorded fragile tissue sarcomas.

1.2.4 Appearances

Signs & appearances change as demonstrated by tumor site, & estimate is immovably connected to the range of the basic tumor. Standard site of metastasis consolidate the lungs, bone marrow, & bones. There are various plan systems for RMS & a collection of described histological sorts. RMS can occur in any sensitive tissue site in the body; the most generally perceived fundamental districts are genitourinary (24%), parameningSBC (16%), farthest point 19%), circle (9%), other head & neck (10%), & arbitrary distinctive goals (22%).

Embryonal rhabdomyosarcoma (ERMS) is the most well-known histological variation, including roughly 60-70% of adolescence cases. It is most regular in kids 0–4 years of age, amid a greatest detailed frequency of 4 cases for each 1 million youngsters. ERMS is described by axle molded cells amid a stromal-rich appearance, & the morphology is like the creating muscle cells of a 6-8 week old developing life. Tumors frequently introduce in the head & neck & in addition the genitourinary track. Alveolar rhabdomyosarcoma (ARMS) is the second most basic sort. ARMS contains roughly 20-25% of RMS-related tumors, & it is similarly appropriated among all age bunches amid a rate of around 1 case for each 1 million individuals ages 0 to 19.Anaplastic rhabdomyosarcoma, is characterized by the nearness of anaplastic cells amid substantial, lobate hyperchromatic cores & multipolar mitotic figures.

1.2.5 Treatment

Rhabdomyosarcoma is a multidisciplinary work on including the utilization of surgery, chemotherapy, radiation, & potentially immunotherapy.There are two principle strategies for chemotherapy treatment for RMS. There is the VAC regimen, comprising of vincristin, actinomyocin D, & cyp, & the IVA regimen, comprising of ifosfamide, vincristin & actinomyocin[15-18].

1.3 Immunology related cancer and its treatment

1.3.1 Immunomodulation

Immunomodulation has been process modifying immune response administration of drug. Many proteins, amino acids & natural compounds have shown a significant ability to regulate immune responses including interferon-γ & steroids. These are biological / synthetic substances could stimulate suppress / modulate any of the immune system including both adaptive & innate arms of the immune response.

1.3.2 Immunotherapy

Immunotherapy is the treatment of disease by inducing, enhancing, or suppressing an immune response. Immunotherapy is utilized to restore the immune system of people amid immune deficiencies such as Cytokines, Interleukin-7 & Interleukin-2.Anti-microbial immunotherapy, involves in activating the immune system which responds to infectious agent. Immunotherapy is utilized to treat allergy & asthma.

1.3.3 Cell-based immunotherapy

Cell-based immunotherapies are effective for some cancers in which immune effect or cells such as lympphocytes, macrophages, dendriticcells, naturalkillercells, & cytotoxic T lymphocytes work together to defend the body against cancer by targeting abnormal antigens expressed on the surface of tumor cells. Therapies such as granulocyte colony-stimulating factor, interferon, & cellular membrane fractions from bacteria are licensed for medical use.

1.3.4 Cancer immunotherapy

Cancer immunotherapy is utilized to stimulate the immune system to destroy tumors. Randomized controlled studies in different cancers results shows increase in the survival from the disease was reported & its efficacy is improved by 20–30%.Immunedevelopment therapies are utilized to treat against Hepatitis & chronic fatigue syndrome[18-24].

1.3.5 Immunosuppressive drugs

Immunosuppressive drugs help to manage organ transplantation & autoimmune disease & the Immune response depends on lymphocyte proliferation. Glucocorticoids are more specific inhibitors of lymphocyte activation which specifically target T lymphocyte activation. Immune tolerance therapy is utilized to reset the immune system in the body by attacking its organs in transplantation. Immunomodulatory drugs are a group of drugs that contains thalidomide, lenalidomide, pomalidomide & apremilast are utilized in the treatment of cancer & autoimmune conditions such as acutemyeloidleukemia, erythema & myelofibriosis.

1.3.6 Immunoadjuvants

Immunoadjuvants are utilized for enhancing vaccines efficacy & consider as specific immune stimulants eg: Freunds adjuvant.These immunoadjuvants are the modulators of immune response. Immunostimulants are utilized to develop resistance against infection by prophylactic agents & produce natural immune response.

1.3.7 Immunodeficiency

Immunodeficiencies occur when one or more components of the immune system are inactive. The ability of the immune system which responds to pathogen will begin to decline at 50 years of age due to Malnutrition, obesity, & alcoholism. Immunodeficiencies can also be inherited acquired. Chronic granulomatous disease, where phagocytes have a reduced ability to destroy pathogens, is an example of an inherited, immunodeficiency. AIDS & cancer cause acquired immunodeficiency. Immunogenicity is the capacity of antigen moves direction on immune response body induce humoral or cell mediated immune responses. Immunogenicity has related amid vaccines of n antigen provides immune response against the pathogen such virus, & bacteria[25-32].

1.3.8 Immunology

Immunology has branch biomedical science gives thought regarding invulnerable frameworks all angles, for example, immune system maladies, excessive touchiness & safe lack. Immunology has applications various orders solution especially fields organ transplantation, oncology, virology, bacteriology, parasitology, psychiatry & dermatology. The imperative lymphoid organs resistant frameworks were thymus, bone marrow, spleen, lymph hubs, & liver. Traditional immunology investigation has been expressed transmission & medication tells about relationship between body frameworks, pathogens & insusceptibility. Clinical immunology is the investigation of ailments brought on by clutters of the invulnerable framework.

1.3.9 Symptomatic immunology

It is the investigation of neutralizer & antigen in which counter acting agent is an incredible instrument for the location of substances by an assortment of indicative methods for example, immunoblotting, and ELISA & immunohistochemical recoloring.

1.3.10 History of Immunology

Starts from pharmaceutical & early reviews were reasons for invulnerability to infection. Soonest known specify of resistance was amid the torment of Athens in 430 BC. Thucydides found that individuals who had recuperated from a past assault of the infection could look after the wiped out without getting the ailment a moment time. In the eighteenth century, Pierre-Louis made trials amid scorpion venom & watched that specific puppies & mice were resistant to this venom. Perception of obtained insusceptibility was later clarified by advancement of immunization & proposed germ hypothesis of illness[33]. Infections were affirmed as human pathogens 1901, amid the disclosure of the yellow fever infection.

1.3.11 Classification of anticancer drugs

Drugs are classified according to the BC Cancer Agency Monographs, unless otherwise specified . Subclassifications are in brackets where applicable.

Alkylating Agents have reactive groups (usually alkyl) that attach to DNA or RNA, leading to interruption in synthesis of DNA, RNA, or proteins.

Bendamustine (nitrogen mustard)

Busulfan (alkyl sulfonate)

Carboplatin (platinum)

Carmustine (nitrosurea)

Chlorambucil (nitrogen mustard)

Cisplatin (platinum)

Cyclophosphamide (nitrogen mustard)

Dacarbazine (triazine)

Estramustine (nitrogen mustard with 17-beta-estradiol)

Hydroxyurea

Ifosfamide (nitrogen mustard)

Lomustine (nitrosurea)

Mechlorethamine (nitrogen mustard)

Melphalan (nitrogen mustard)

Oxaliplatin (platinum)

Procarbazine (triazine)

Streptozocin (nitrosurea)

Temozolomide (triazine)

Thiotepa (aziridine)

Treosulfan

Antimetabolites are structural analogues of naturally occurring molecules required for DNA and RNA synthesis. When substituted for the natural body substances, they disrupt DNA and RNA synthesis. Azacitidine (pyrimidine analogue)

Capecitabine (pyrimidine analogue)

Cladribine (adenosine analogue)

Cytarabine (pyrimidine analogue)

Fludarabine (purine analogue)

Fluorouracil (pyrimidine analogue)

Gemcitabine (pyrimidine analogue)

Mercaptopurine (purine analogue)

Methotrexate (folate analogue)

Pemetrexed (folate analogue)

Pralatrexate (folate analogue)

Raltitrexed (folate analogue)

Thioguanine (purine analogue)

Topoisomerase Inhibitors (I and II) cause DNA strand breaks by disrupting the function of topoisomerase enzymes, which are responsible for regulating the 3-D structure of DNA. Topoisomerase I irinotecan

Topotecan

Anti microtubule Agents (Mitotic Inhibitors) inhibit cell mitosis by interfering with microtubule formation or function.

cabazitaxel (taxane)

docetaxel (taxane)

eribulin

ixabepilone

paclitaxel (regular and nanoparticle, albumin-bound) (taxane)

vinblastine (vinca alkaloid)

vincristine (vinca alkaloid)

vinorelbine (vinca alkaloid)

Topoisomerase II amsacrine

anthracyclines - daunorubicin - doxorubicin (regular and pegylated liposomal) - epirubicin - idarubicin etoposide

mitoxantrone

teniposide

Miscellaneous Antineoplastics - Refer to BC Cancer monographs for pharmacology. arsenic trioxide

Asparaginase

Bleomycin

Belinostat

Dactinomycin

Iniparib

Mitomycin

Mitotane

Porfimer

Romidepsin

vorinostat

Antiestrogens oppose the effects of estrogen. tamoxifen – partial estrogen antagonist (antagonist on breast tissue, agonist on endometrium, bone and lipids) fulvestrant – full estrogen antagonist (no agonist activity) Aromatase Inhibitors (AIs) prevent the final step in the conversion of androgens to estrogens in peripheral tissues.

Anastrozole

Exemestane

letrozole

Luteinizing Hormone Releasing Hormone (LHRH) Agonists (also known as gonadotropin releasing hormone analogues) initially stimulate the release of luteinizing hormone, which leads to an increase in sex hormones (testosterone, estradiol). Chronic use leads to down-regulation of the LHRH receptors, leading to decreased testosterone in men and estrogen in women. Buserelin

Goserelin, leuprolide.

Antiandrogens opposes the effects of androgens. Apalutamide, bicalutamide, enzalutamide – more affinity for androgen receptors and Plus, inhibits more steps in the androgen inhibition than other agents in this class flutamide, nilutamide, Androgen

Biosynthesis Inhibitors abiraterone - selectively inhibits the enzyme (CYP17) that, converts pregnenolone and progesterone into testosterone precursors. Androgens testosterone - The exact mode of action for androgen therapy in breast cancer is unclear. Corticosteroids are thought to act via apoptosis induction. Dexamethasone, prednisone, Somatostatin Analogues inhibit exocrine and endocrine secretion of hormones, which is useful for hormone-secreting tumours (e.g., neuroendocrine). Additional mechanisms include modulation of biliary/GI motility and apoptosis inductions. Lanreotide, octreotide.

Luteinizing Hormone Releasing Hormone (LHRH) Antagonist (also known as gonadotropin releasing hormone antagonist) reduce the release of luteinizing hormone, follicle-stimulating hormone, and consequently testosterone by the testes. Degarelix, Progestins suppress the release of luteinizing hormone from the pituitary gland and subsequently decrease estrogen levels. Additional mechanisms include binding to progesterone, glucocorticoid, and androgen receptors, resulting in decreased number of estrogen receptors and decreased estrogen and progesterone levels peripherally in target tissues. Medroxyprogesterone, megestrol, Prolactin Lowering Agents are dopamine antagonists that decrease hormone production and the size of prolactin-dependent pituitary adenomas by inhibiting the release and synthesis of prolactin from the anterior pituitary. Bromocriptine, cabergoline, quinagolide, Thyrotropin Stimulating Hormone Agonist is a recombinant thyrotropin used for serum thyroglobulin testing in thyroid cancer. thyrotropin alpha.

Cytokines are proteins that are involved in the cell signaling that leads to immune responses at sites of inflammation, infection, and trauma. They induce various cellular responses, such as suppression of cell proliferation and augmentation of the cytotoxicity of lymphocytes. Aldesleukin, interferon, peginterferon, Vaccine Therapy bacillus calmette-guerin (BCG) - a live, attenuated bacteria (Mycobacterium bovis) that exerts a variety of antitumour actions, including induction of a local granulomatous reaction, activation of histiocytes, and other direct and indirect stimulation of immune responses. The result is a local inflammatory response that destroys tumour cells.

Immunomodulatory Drugs (IMIDs) have multiple mechanisms of action, including inhibition of proliferation of certain hematopoietic tumour cells, enhancing numbers and activity of T, NK, and NK T cells, and inhibition of angiogenesis. Lenalidomide, pomalidomide, thalidomide, Differentiating Agents are vitamin A derivatives. Their proposed mechanism of action is to overcome impaired cellular differentiation. Acitretin, bexarotene, tretinoin, Other Immunotherapies imiquimod – TLR7 agonist, Monoclonal antibodies could also be considered immunotherapies, particularly those that inhibit CTLA-4, PD-1 or PD-L1 (Checkpoint Inhibitors), or IL-6. They are covered on the pages that follow.

Targeted therapies target receptors, ligands, or intracellular molecules involved in the signal transduction of cancer cells. The following table is a listing of targeted therapies with the target(s) listed in brackets. See the following page for more information on targets. Note that the relative affinity to particular targets is not always clear for each agent, and may differ when used in different indications. Some of the available literature refer to drugs by their target, such as EGFR-inhibitors or multikinase inhibitors for oral drugs with multiple targets (e.g., pazopanib,sorafenib, sunitinib). afatinib (EGFR, HER2, HER4) AGS-16C3F (antibody conjugated dinutuximab (GD2) durvalumab (PD-L1) pembrolizumab (PD-1) pertuzumab (HER2) with cytotoxic) erlotinib (EGFR) ramucirumab (VEGFR2 and VEGF A, C, and D) alectinib (ALK) everolimus (MTOR) regorafenib (VEGFR-1, -2 & -3, TIE2, KIT, RET, alemtuzumab (CD52) gefitinib (EGFR) RAF-1, BRAF, BRAFV600E, PDGFR, FGFR) atezolizumab (PD-L1) ibrutinib (BTK) ribociclib (CDK 4/6) avelumab (PD-L1) idelalisib (PI3Kδ) rituximab (CD20) axitinib (VEGFR 1, 2, & 3) imatinib (BCR-ABL, PDGF, c-KIT) ruxolitinib (JAK 1 & 2) bevacizumab (VEGF) inotuzumab ozogamicin (CD22) (antibody siltuximab (IL-6) blinatumomab (CD3 & CD19) conjugated with cytotoxic) sorafinib (c-Raf, b-Raf, V600E b-Raf, KIT, FLT-3 bortezomib (26S proteosome) ipilumumab (CTLA-4) VEGFR -2, -3 & -beta) brentuximab vedotin (CD30) (antibody lapatinib (EGFR, HER2) sunitinib (VEGFR 1, 2, & 3, PDGFR α & β), KIT, conjugated with cytotoxic) lenvatinib (VEGFR, FGFR, PDGFRα, KIT, RET) FLT-3, CSF-1R, RET) cabozantinib (c-Met, VEGF, FLT3) carfilzomib (26S proteosome) midostaurin (FLT-3, KIT, PDGFR) nilotinib (BCR-ABL, c-KIT, PDGFR) temsirolimus (MTOR) tocilizumab (IL-6) carotuximab (also known as

TRC105) (CD105) nivolumab (PD-1) trametinib (MEK 1 & 2) cemiplimab (PD-1) obinutuzumab (CD20) trastuzumab (HER2) ceritinib (ALK) ofatumumab (CD20) trastuzumab emtansine (HER2) (antibody cetuximab (EGFR) olaparib (PARP-1, PARP-2, PARP-3) conjugated with cytotoxic) cobimetinib (MEK) olaratumab (PDGFR α) vandetanib (VEGFR-2, EGFR, RET) crizotinib (ALK, HGFR, C-Met, ROS1) osimertinib (EGFR) vemurafenib (BRAF) dabrafenib (BRAF) panitumumab (EGFR) venetoclax (BCL-2) daratumumab (CD38) palbociclib (CDK 4/6) vismodegib (Hh)

2.0 LITERATURE REVIEW

Bargoni A, et al., (2012)[35] observed bone marrow microenvironment provides a site for cancer cells to evade systemic anticancer therapy. Dormant tumor micrometastases are believed to be the source of disease persistence and relapse; however, the exact characteristics of cancer stem cells vs. cancer cells with limited metastatic potential have yet to be elucidated. Bisphosphonates inhibit osteoclast-mediated bone resorption, are approved for treating malignant bone disease from advanced cancers, and have shown efficacy for preventing cancer treatment-induced bone loss. Altering the bone marrow microenvironment to make it less conducive to cancer cell survival is now emerging as an important means to prevent cancer recurrence. This review aims to distill the diverse literature and provide a brief overview of the numerous preclinical and early clinical studies of bisphosphonates demonstrating a variety of direct and indirect anticancer activities that affect both the tumor cell (the "seed") and surrounding microenvironment (the "soil"). Recently, zoledronic acid was found to improve disease-free survival and overall survival in some adjuvant breast cancer settings and prolonged survival in patients with multiple myeloma and other advanced cancers. In the prostate cancer setting, antiresorptive therapy was reported to delay the development of overt bone metastases. Ongoing studies will provide further insight regarding the anticancer potential of bisphosphonates and other antiresorptive agents.

Benoit JP, et al., (2012)[36] studied *Carica papaya* is widely cultivated in tropical and subtropical countries and is used as food as well as traditional medicine to treat a range of diseases. Increasing anecdotal reports of its effects in cancer treatment and prevention, with many successful cases, have warranted that these pharmacological properties be scientifically validated. A bibliographic search was conducted using the key words “papaya”, “anticancer”, and “antitumor” along with cross-referencing. No clinical or animal cancer studies were identified and only seven in vitro cell-culture-based studies were reported; these indicate that *C. papaya* extracts may alter the growth of several types of cancer cell lines. However, many studies focused on specific compounds in papaya and reported bioactivity including anticancer effects. This review summarizes the

results of extract-based or specific compound-based investigations and emphasizes the aspects that warrant future research to explore the bioactives in *C. papaya* for their anticancer activities.

Bergelson L, et al, (2005)[37] have entitled that the counter tumor impacts of thalidomide have been related amid it's against antigenesis properties. Second era thalidomide analogs are unmistakable mixes amid improved restorative potential. In spite of the fact that these mixes are starting to enter trials for the treatment of growth there is almost no data amid respect to the counter angiogenic action of these are clinically significant compound. Besides, it is not known how the different immunomodulatory exercises of these mixes identify amid hostile to angiogenic movement. In this review we evaluated the counter angiogenic action of mixes from both IMiD™ & SelCID™ classes of analogs utilizing a novel in vitro multicellular human examine framework & the built up rodent aorta measure. Our outcomes demonstrate that both the IMiDs & SelCIDs tried are fundamentally more strong than thalidomide. The counter angiogenic power of the analogs was not identified amid hindrance of endothelial cell expansion, nor their TNF-α/PDE sort 4 inhibitory properties. In any case, against transient impacts in vitro & restraint of tumor development in vivo was seen amid the simple IMiD-1.Our outcomes demonstrate that hostile to angiogenic action traverses both at present characterized classes of thalidomide simple & is not identified amid their already portrayed immunomodulatory properties. Distinguishing proof of the differential impacts of these mixes will empower focusing of such mixes into the fitting clinical setting.

Bunjes H, et al, (2005)[38]have indicated colloidal gold nanocrystals have been utilized to build up another class of nanobiosensors that can perceive & identify particular DNA arrangements & single-base transformations in a homogeneous organization. At the center of this biosensor is a 2.5-nm gold nanoparticle that capacity as both a nano-framework & a nano-quencher (proficient vitality acceptor). Connected to this center are oligonucleotide particles named amid a thiol assemble toward one side & a fluorophore at the other. This cross breed bio/inorganic develop is found to suddenly gather into an obliged curve like adaptation on the molecule surface. Authoritative of target atoms

brings about a conformational change, which reestablishes the fluorescence of the extinguished fluorophore. Dissimilar to ordinary sub-atomic reference points amid a stem-&-circle structure, the nanoparticle tests don't require a stem, & their experience fluorescence builds little amid temperature. In correlation amid the, metal Nan Ps have remarkable auxiliary & optical properties for new applications in biosensing & atomic designing.

Bala I, et al.,(2016)[34] detailed the cancer is a major public burden in both developed and developing countries. Anticancer activity is the effect of natural and synthetic or biological and chemical agents to reverse, suppress or prevent carcinogenic progression. Several synthetic agents are used to cure the disease but they have their toxicity and hence the research is going on to investigate the plant derived chemotherapeutic agents. Therefore an attempt has been made to review some medicinal plants having anticancer properties. In this review, anticancer medicinal plants of Indian origin belonging to various families are reported along with detailed information. All these plants are potential candidates for advanced studies since they are showing good anticancer activity. The present paper is a comprehensive review of different literature sources. It will be helpful to explore the medicinal value of the plants against the cancer and for the new drug discovery from them for the researchers and scientists around the world.

Simpson CA, et al, (2005)[39] have explained that Magnetite Nan Ps were set up by coprecipitation of Fe2 & Fe3 amid NH4OH, & afterward, amino silane was covered onto the surface of the magnetite Nan Ps. Transmission electronic microscopy demonstrates the normal size of 7.5 nm in distance across. Powder X-beam diffraction & electronic diffraction estimations demonstrate the spinel structure for the magnetite Nan Ps. FT/IR spectra show that amino silane atoms have been bound onto the surface of the magnetite Nan Ps by Fe/O/Si substance bonds. Vitality dispersive X-beam spectroscopy shows nuclear proportion of 96.75:3.25 for Fe:Si, inferring an about monolayer covering of amino silane on the magnetite molecule surface as per a harsh computation. By a chemical connected examine, it was demonstrated that the amino silane-covered magnetite Nan Ps could essentially enhance the protein immobilization.

Huffman A, et al., (2010)[40]have expressed that lessened measurements materials show attributes very not quite the same as their mass conduct. Strikingly, most infections, microorganisms, pathogens, particles in gas stage & other chemical–biological specialists, which frame the premise of this examination, likewise have practically identical measurements. Our present & progressing examination is pointed towards the discovery of substance & natural specialists utilizing nanostructured materials. We have examined nanotubes, Nan Ps, nanowires, & nanoporous materials for biocompatibility & resulting recognition. Likewise, in light of our field discharge contemplates on carbon nanotubes, we have recommended gadget plans to recognize natural outflow. Discovery systems & preparatory information from electrochemical sensors, nuclear constrain microscopy, & surface plasmon reverberation is introduced for the identification of chemical–biological specialists immobilized on layers of Nan Ps. As a basic stride in the advancement of sensors/locators, methodologies for surface functionalization & immobilization for carbon nanostructures, Nan Ps, & nanoporous materials are likewise displayed. Such gadgets show special attributes, morphological adaptability, & biocompatibility. The inevitable target of our examination is to build up a NT based sensor stage that will empower the direct electrical, optical, or electro-optical recognition of natural & substance specialists in a name free, exceptionally multiplexed arrange over a wide element run.

Shen H, et al, (2012)[41] explored Antioxidant action of chose business Seaweeds. Four sorts of ocean growth to be specific Nori (Porphyrasp.), Kumbu (Laminariasp.), Wakame (Undariasp.) & Hijiki (Hijikiasp.) were utilized as a part of the review. The concentrates were set up amid water & ethanol, individually. The β-carotene blanching & 1,1-diphenyl-2-picrylhydrazyl (DPPH) measures were utilized to decide cell reinforcement properties of kelp. From the outcomes Wakame showed the most astounding cancer prevention agent & free radical rummaging exercises in ethanolic remove. The outcomes demonstrated that handled business ocean growth displayed noteworthy aggregate cancer prevention agent & free radical searching exercises.

Falugi C, et al., (2012)[42] revSBCed Free-radical searching limit & lessening force of wild consumable mushrooms from upper east Portugal.Individual top & stipe activity.Methanolic extricates from the whole mushroom, the top & the stipe, independently, were screened for their decreasing force & free radical rummaging limit by substance examines. The aggregate phenolic substance was resolved, keeping in mind the end goal to evaluate its impact on the concentrate's cancer prevention agent movement. Both two species demonstrated cell reinforcement potential; yet L. Deliciosus ended up being more dynamic. The bit of the mushroom utilized had an impact on the outcomes got, amid the top methanolic removes showing the best cancer prevention agent impact.

Liu CH, et al, (2005)[43] contemplated Antioxidant movement, biokinetics, & bioavailability of Vitamin E.α tocopherol is a wonderful chain-breaking cell reinforcement that has all the earmarks of being the main significant lipid-dissolvable cancer prevention agent of its kind in mammalian layers & lipoproteins. Investigations of the biokinetics & bioavailability of vitamin E demonstrated that vitamin E turnover is slowest in neural & mind tissues. It is along these lines vitamin E assumes a critical part in keeping up neurological capacity in man.

Wingard CJ, et al., (2011)[44] examined Invitroimmunomodulatory impacts of thai restorative plants on the mitogen animated multiplication of human fringe blood mononuclear cells.The immunomodulatory impacts of Thai therapeutic plants, including Murdannialoriformis, Cymbopogoncitratus, Momornicacharantia, Centellaasiatica, Allium sativum, Carthamustinctorius, Eclipta alba, Cyperusrotundus, lotus dust (Dee-Buo), & plant incipient organisms in seeds of the lotus (Ke-Sorn-Buo), on the mitogen empowered expansion of human fringe blood mononuclear cells (PBMCs) were explored. The outcomes got from that review showed that lone water separates from C. asiatica had an immunostimulating impact on mitogen-invigorated expansion of human PBMCs. Interestingly, the ethanol extricate from this plant demonstrated immunosuppressive action.

Janway C, et.al, (2005)[45] assessed Low-thickness lipoprotein cell reinforcement action of phenolic mixes & polyphenol oxidase action in chose clingstone peach cultivars. The cell reinforcement capability of eight clingstone peach cultivars was researched by deciding phenolic mixes & restraint of low-thickness lipoprotein (LDL) oxidation. Cultivars low in polyphenol oxidase (PPO) was likewise chosen to limit enzymatic searing. From the aftereffects of study it was observed that All eight clingstone peach cultivars exhibited great cancer prevention agent action in the hindrance of LDL oxidation. Huge contrasts were found in individual phenolic mixes & PPO exercises of all cultivars. The Kakamas, Walgant, & 18-8-23 cultivars demonstrated the most noteworthy rates of hindrance of LDL oxidation & the least PPO exercises.

Kim CK, et al, (2009)[46] assessed Total Antioxidant movement & fiber substance of select florida-become tropical fruits.Fourteen tropical organic products from south Florida (red guava, white guava, carambola, red pitaya (red dragon),white pitaya (white mythical serpent), mameysapote, sapodilla, lychee, longan, green mango, ready mango,green papaya, & ready papaya) were assessed for cell reinforcement action, add up to dissolvable phenolics (TSP),total ascorbic corrosive (TAA), add up to dietary fiber (TDF), & pectin. ORAC (oxygen radical absorbancecapacity) & DPPH (1,1-diphenyl-2-picrylhydrazyl, radical searching action) tests were utilized todetermine cell reinforcement action. The cell reinforcement exercises assessed by both ORAC & DPPH indicated comparable patterns where red guava & carambola displayed the most elevated & sapodilla & green papaya showed the least levels. From consequences of study Guava & mamely sapote displayed the most elevated TDF & pectin levels.

Lemasurier G, et.al, (2012)[47] directed a Comparative investigation of ABTS, DPPH, FRAP, & ORAC tests for evaluating cancer prevention agent movement from guava natural product removes. Guava natural product concentrates were examined for cell reinforcement action measured in methanol extricate (AOAM), cancer prevention agent action measured in dichloromethane separate (AOAD), ascorbic corrosive, add up to phenolics, & aggregate carotenoids substance. Ascorbic corrosive & phenolics are the significant givers to cancer prevention agent action in guava organic product. The ABTS,

DPPH, FRAP, & ORAC examines gave similar outcomes for the cancer prevention agent movement measured in methanol concentrate of guava natural product separates. The FRAP method demonstrated high reproducibility, was basic, quickly performed & demonstrated the most astounding relationship amid both ascorbic corrosive & aggregate phenolics. In this manner, FRAP method would be a fitting system for deciding cell reinforcement in guava natural product extricate.

Loo C, et al, (2006)[48] examined Antioxidant action & aggregate phenolics in chose natural products, vegetables, & grain products.The cancer prevention agent exercises & aggregate phenolics of 28 plant items, including sunflower seeds,flaxseeds, wheat germ, buckwheat, & a few organic products, vegetables, & therapeutic plants were resolved. From that review it was shown that components other than aggregate phenolics can assume a noteworthy part in the cancer prevention agent movement of plant materials, for example, seabuckthorn.

Malcolmson C, et al., (2006)[49] considered Immunomodulatory & Antimicrobial Effects of Some Traditional Chinese Medicinal Herbs.Theyreported on seven Chinese herbs, (Aloe veraMill. (Aloaceae),Angelica species (Umbelliferae), AstragalusmembranaceusBunge.(Leguminosae),Ganodermalucidum(Fr.)Karst.(Ganoder mataceae), Panax ginseng C.A Mey.(Araliaceae), Scutellaria species (Lamiaceae) & Zingiber officinale Rosc.(Zingiberaceae) amid accentuation to their immunomodulatory & antimicrobial exercises. The fruitful derivationof unadulterated bioactive mixes from Ganodermalucidum, ginseng & Zingiberofficinale bolsters the customary routine of utilizing these plants to invigorate the insusceptible framework**.**

Sacchetti C, et al, (2006)[50] assessed Antioxidant & Immunomodulatory constituents of Henna clears out. Seven mixes were confined embracing the lymphocyte change measure guided fractionation of the aggregate methanolic concentrate of henna (LawsoniainermisL.) takes off. Seven mixes were disengaged, five from the chloro formic part & additionally two mixes from the ethyl acetic acid derivation fraction.The cell-intervened insusceptible reaction wasdetermined in the fringe blood lymphocytes

(PBL) because of mitogenic incitement utilizing either phytohaemagglutinin (PHA) or concanavalinA (Con An) as mitogens that invigorate human T-& B-cells however T-cells all the more enthusiastically. It was found that the immunostimulant action of the aggregate methanolic concentrate of henna leaves is more noteworthy than that of individual dissolvable parts at a similar focus (1 mg/ml), recommending a synergism between the diverse segments in each portion.

Tojo C, et al, (2010)[51] have entitled that the dependability & execution of a local cooler amid Nan Ps in the working liquid was examined tentatively. Mineral oil amid TiO2 Nan Ps blends were utilized as the oil rather than Polyol-ester oil in the 1, 1, 1, 2-tetrafluoroethane refrigerator.The similarity of nonmetallic materials in the framework amid the HFC134a & mineral oil–Nan Ps blends was contemplated before the cooler execution tests. The cooler execution amid the Nan Ps was then examined utilizing vitality utilization tests & stop limit tests. The outcomes demonstrate that HFC134a & mineral oil amid TiO2 Nan Ps works typically & securely in the cooler. The fridge execution was superior to the HFC134a & POE oil framework, amid 26.1% less vitality utilization utilized amid 0.1% mass part TiO2 Nan Ps contrasted amid the HFC134a & POE oil framework. Similar tests amid Al2O3 Nan Ps demonstrated that the distinctive Nan Ps properties have little impact on the icebox execution. In this manner, Nan Ps can be utilized as a part of household coolers to impressively lessen vitality utilization.

Nooman, et al, (2008)[28] assessed Antioxidant movement of some regular plants. The methanolic rough concentrates of some regularly utilized therapeutic plants were screened for their free radical searching properties utilizing ascorbic corrosive as standard cancer prevention agent. Consequences of that review demonstrated that general cancer prevention agent movement of green tea (Camellia sinensis Linn.) was the most grounded, followed in sliding request by dark tea (Camellia sinensis Linn.), Eugenia caryophyllus (Spreng.) Bullock & Harrison, Piper cubeba Linn. ,Zingiber officinale Roscoe & Piper nigrum Linn. Trigonellafoenumgraecum Linn.& Elettariacardamomum (Linn.) Maton indicated feeble free radical rummaging movement amid the DPPH strategy.

Huang CY, et al, (2007)[52] have foucused that ligament powder & chondroitin sulfate can produce gold or silver Nan Ps from arrangements of chloroauric corrosive trihydrate or silver nitrate individually. These perceptions provoked us to estimate that the mitigating impacts saw amid the aurotherapy of rheumatoid joint inflammation may be expected to the in vivo era of Au NPs. To test this speculation we integrated Au NPs or Ag NPs utilizing CT or CS & assessed their immunomodulatory potential in a characteristic executioner (NK) cell movement test. Likewise, tests were sent to partners to be tried in an embryonic zebrafish measure to assess their mitigating possibilities. Comes about because of the zebrafish measures show little lethality from presentation to the Au NPs or Ag NPs arrangements & the size of the fiery reaction was essentially diminished amid in the sight of Au NPs or Ag NPs combined amid CS or CT. Au NPs or Ag NPs combined amid CS diminished the cytotoxic action of NK cells towards tumor cells; in any case, Ag NPs ended up being cytotoxic towards the NK cells. Bright & noticeable spectroscopy, inductively coupled plasma optical emanation spectroscopy, flame nuclear ingestion spectroscopy, dynamic light disseminating, gel penetration chromatography & transmission electron microscopy were utilized to describe the NPs.

Casal JI, et al, (2009)[53] have entitled Nan Ps have one of a kind physicochemical properties which make them promising stages for medication conveyance. In any case, safe cells in the circulation system & in tissues have a penchant to immerse & dispose of certain Nan Ps. A nanoparticle's association amid plasma proteins & blood parts may impact take-up & freedom & henceforth conceivably influence conveyance & conveyance to the planned target destinations. Nanoparticle take-up by the invulnerable cells is impacted by many variables. Diverse Nan Ps have been appeared to follow up on various pathways, while different attributes/properties likewise influence which pathway is utilized for molecule disguise. Nanoparticle protein restricting happens momentarily once the molecule enters organic medium, & the physical properties of such a particle–protein complex are regularly not quite the same as those of the detailed molecule. These new properties can add to various natural reactions & change nanoparticle biodistribution. In this manner, in the circumstance when particular conveyance to insusceptible cells is not fancied, the perfect nanoparticle stage is the one whose honesty

is not aggravated in the complex natural environment, which gives stretched out course in the blood to boost conveyance to the objective site, is not dangerous to blood cell segments, & is imperceptible to the invulnerable cells which can expel it from dissemination. This audit talks about the latest information on nanoparticle communications amid blood segments & how molecule size & surface charge characterize their hematocompatibility. This incorporates properties which decide molecule communication amid plasma proteins & take-up by macrophages. We will likewise give an outline of in vitro strategies valuable in distinguishing connections amid segments of the insusceptible framework & the potential impacts of such collaboration on molecule dissemination to tissues.

Cavalli R, et al, (2009)[54] have indicated that the impact of size & convergence of Nan Ps on the viable gas–liquid surface pressure of fluid arrangements of bismuth telluride Nan Ps functionalized amid thioglycolic corrosive. The gas–liquid surface pressure is acquired by explaining the Laplace–Young condition under tentatively measured limit conditions & bead parameter

Chapple R, et al, (2009)[55] have foucused Nan Ps speak to a promising medication conveyance arrangement of controlled & focused on medication discharge. They are exceptionally intended to discharge the medication in the region of target tissue. The point of this review was to plan & assess polymethacrylic corrosive Nan Ps containing lamivudine in various medications to polymer proportion by nanoprecipitation technique. SEM demonstrated that Nan Ps have a discrete round structure without total. The normal molecule size was observed to be 121 + 8 - 403 + 4 nm. The molecule size of the Nan Ps was bit by bit expanded amid increment in the extent of polymethacrylic corrosive polymer. The medication substance of the Nan Ps was expanding on expanding polymer fixation up to a specific focus. No apparent contrast was seen in the degree of debasement of item amid 60 days in which, Nan Ps were put away at different temperatures. FT-IR thinks about showed that there was no synthetic connection amongst medication & polymer & security of medication. The in-vitro discharge conduct from all the medication stacked groups was observed to be zero requests & gave managed discharge over a time

of 24 h. The created definition overcome & mitigates the disadvantages & constraints of lamivudine managed discharge details & could probability be invaluable regarding expanded bioavailability of lamivudine.

Chen DB, et al, (2001)[56] have indicated immunomodulatory impacts of little inorganic Nan Ps & the effect of test plan in that. Gold, cobalt oxide & iron oxide Nan Ps were integrated in arrangement under conditions that guaranteed monodispersed & stable particles in solvents & when weakened in cell culture medium. Particles & solvents were tried for their cytotoxic & cytokine administrative consequences for deified & essential human lung epithelial cells in the nonappearance & nearness of the master incendiary cytokine TNF-α. The molecule suspensions & solvents were not cytotoxic, but rather a noteworthy impact on cytokine enlistment because of the synthetic solvents was watched, despite the fact that these are routinely utilized as a part of Nan Ps amalgamation. Noteworthy immunomodulatory impacts of some molecule sorts on the deified epithelial cells were watched, these impacts were more articulated in essential epithelial cells. All in all, the dissolvable utilized to set up the Nan Ps & the decision of cell sort can influence the result of nanotoxicological studies.

PLANT PROFILE

Strobilanthes consanguineous, often known as common madder or Indian madder, is a species of flowering plant in the coffee family, Acanthaceae . It has been cultivated for a red pigment derived from roots.

Accepted Name:

Strobilanthes consanguineus

Family:

Acanthaceae

Used in:

Folk

Kingdom: Plantae

Pylum: Tracheophyta

Class: Magnoliopsoda

Order: Lamiales

Family: Acanthaceae

Genus: Strobilanthes

Species: consanguineus

Family: Acanthaceae

Description: Erect shrubs, 1-2 m tall. Leaves opposite, 10-17 x 5-10 cm, nearly glabrous, dentate, ovate-lanceolate, acuminate at apex, cuneate at base, more prominently toothed; main nerves 7-8 pairs, subparallel. Spikes more slender, more interrupted, nearly glabrous, 5-8 cm long, short-peduncled. Flowers white in paniculate spikes; bracts larger, subulate, hairy, acuminate; bracteoles linear, short. Calyx .6 cm long, the lobes slender. Corolla 1.5 cm long, glabrous without. Stamens 2 fertile, hardly monadelphous, though sometimes connected at base; anthers oblong, muticous, 2-celled. Disk small or as a stalk to the ovary. Ovary 2-celled, ovules 2 in each cell; style linear; stigma of one linear branch, the other suppressed or a mere point.

Capsules ca. 9 mm long; seeds much compressed, glabrous, densely hairy when wetted, with a basal areole.

Habit: Shrub

Flowering & Fruiting: October-February

District(s): Kozhikkode, Idukki, Malappuram, Thiruvananthapuram, Wayanad

Habitat: Evergreen forests

Distribution: Southern Western Ghats

Flower colour(s): White, Blue

Monocot/Dicot: Dicotyledonous Plants

Endemic to: Southern Western Ghats

Localities: Udumbatheri, Muthappanpuzha

Erect shrubs, 1-2 m tall. Leaves opposite, 10-17 x 5-10 cm, nearly glabrous, dentate, ovate-lanceolate, acuminate at apex, cuneate at base, more prominently toothed; main nerves 7-8 pairs, subparallel. Spikes more slender, more interrupted, nearly glabrous, 5-8 cm long, short-peduncled. Flowers white in paniculate spikes; bracts larger, subulate, hairy, acuminate; bracteoles linear, short. Calyx .6 cm long, the lobes slender. Corolla 1.5 cm long, glabrous without. Stamens 2 fertile, hardly monadelphous, though sometimes connected at base; anthers oblong, muticous, 2-celled. Disk small or as a stalk to the ovary. Ovary 2-celled, ovules 2 in each cell; style linear; stigma of one linear branch, the other suppressed or a mere point. Capsules ca. 9 mm long; seeds much compressed, glabrous, densely hairy when wetted, with a basal areole

It can grow to 1.5 m in height. The evergreen leaves are 5–10 cm long and 2–3 cm broad, produced in whorls of 4-7 starlike around the central stem. It climbs with tiny hooks at the leaves and stems. The flowers are small (3–5 mm across), with five pale yellow petals, in dense racemes, and appear from June to August, followed by small (4–6 mm diameter) red to black berries. The roots can be over 1 m long, up to 12 mm thick. It

prefers loamy soils with a constant level of moisture. Madders are used as food plants for the larvae of some Lepidopteraspecies including Hummingbird hawk moth

Strobilanthes consanguineus was an economically important source of a red pigment in many regions of Asia, Europe and Africa. It was extensively cultivated from antiquity until the mid nineteenth century. The plant's roots contain an organic compound called Alizarin, that gives its red colour to a textile dye known as Rose madder. It was also used as a colourant, especially for paint, that is referred to as Madder lake. The substance was also derived other species; *Rubia tinctorum*, also widely cultivated, and the Asiatic species *Rubia argyi* , based on the Japanese. The invention of a synthesized duplicate, an anthracene compound called alizarin, greatly reduced demand for the natural derivative.

The roots of *Strobilanthes consanguineus* are also the source of a medicine used in Ayurveda; this is commonly known in Ayurvedic Sanskrit as Manjistha (or Manjista or Manjishta) and the commercial product in Hindi as Manjith.

It is known as btsod in Traditional Tibetan Medicine where it is used to treat blood disorders; spread heat, excess heat in the lungs, kidneys, and intestines; reduce swelling; and is a component of the three reds, a subcompound included in many Tibetan preparations in order to remove excess heat in the blood.

- Manjit is a bitter, antiseptic, styptic, anodyne, depurative, and hypotensive drug.
- The plant is also used against blood dysentery, inflammations, and urino-genital disorders.
- It is also an alternative, pigment stimulator, and tonic.
- Manjishtha is a perennial, herbaceous climber with very long, cylindrical roots having a thin red bark.
- Stem is long, rough, slightly woody at the base, quadrangular, and glabrous.
- Branches climb by means of numerous prickles.
- Leaves are heart shaped, about 5–10 cm in size, five-nerved from the leaf base, and occur in whorls of four.
- Petiole is roughly triangular with many sharp recurved prickles on the edges.
- Flowers are small, yellow, and scaly, and occur in terminal cymes.

- Bracts are ovate and leafy.
- Calyx is tubular, less than 1 cm long.
- Corolla is a greenish, divided to the base, tubular with five lobes, and about 3 mm long.
- Fruits are 4–6 mm in diameter, globose, smooth, shining, violet or purple black in colour with grey black seeds.
- Flowering occurs in August–September and fruiting in October–November.
- The species is found throughout the hilly subtropical to sub-temperate regions of India, between 300 m and 2000 m altitudes[57-65].

Figure No. 2: Leaves of *Strobilanthes consanguineus -I*

Figure No. 3: Leaves of *Strobilanthes consanguineus -II*

Figure No.4: Leaves of *Strobilanthes consanguineus -III*

Figure No. 5: Leaves of *Strobilanthes consanguineus -IV*

Figure No. 6: Leaves of *Strobilanthes consanguineus -V*

- Strobilanthes consanguineus occurs mostly in loamy soil rich in humus.

- The rainfall is high in the regions in which this plant grows.
- The plant is a climber and requires support for growth.
- The plant is propagated through seeds and two-node root cuttings.
- The seeds are collected during December and January.
- It is preferable to use seeds for large-scale cultivation, considering the cost factor and high rate of germination.
- The planting stock may be raised in nursery in January through seeds.
- The seeds obtained from dried ripe black fruits are sown in nursery beds either in rows or randomly by broadcasting.
- A thin layer of soil and organic manure is spread over the seeds, and the beds are regularly watered.
- After germination, seedlings with two to three leaves are transplanted in polybags for establishment.
- The plants can also be raised through cuttings containing two or three nodes, treated with commercially available rooting hormones or 3000 PPM (parts per million) IBA (indole-3-butyric acid) for rooting.
- Although cuttings give 90% success, it is still preferable to take up large-scale cultivation through seeds, which is economic and results in 80%–85% germination within 20 days.

Propagule rate and pretreatment

- About 350 g of seeds are required to raise a nursery for planting in 1 hectare of land.
- It is advisable to treat the seeds with 0.02% Bavistin 50 WP before sowing.
- Sometimes, seeds may be directly broadcast in the well-prepared field or sown in rows.
- In such cases, much higher quantities of seeds, to the tune of 1.5–2 kg, may be required.

Indian madder is widely used in traditional medicine.
The roots are alterative, anodyne, antiphlogistic, antitussive, astringent, diuretic, emmenagogue, expectorant, hypotensive, styptic, tonic and vulnerary.

- The soil is properly ploughed, harrowed once or twice, and planked lightly to make it porous and weed- free.
- FYM (farmyard manure) @ 10 tonnes/hectare and NPK (nitrogen, phosphorus, potassium) @ 30:40:20 kg, respectively, are applied to the soil as basal dose during land preparation.

Transplanting and optimum spacing

- Seedlings/rooted cuttings are trans- planted to the main field in April– May.
- An optimum spacing of 60 cm × 75 cm is recommended in the field, which gives an optimum crop stand of 22,000 plants per hectare.
- When the seeds are directly sown in rows or broadcast in the well-prepared field, singling is an important activity to provide optimum spacing to the growing plants.

Intercropping system

- The plant is a climber and may be intercropped with shrubby, perennial species, serving as host/support crop.

Interculture and maintenance practices

- FYM @ 5 tonnes/hectare or nitrogen @ 20 kg/hectare is applied 120–130 days after transplanting by top dressing.
- In the second and third years, NPK may each be applied @ 20 kg/hectare by top dressing with the onset of rainfall after the intercultural operation.
- In the first year, first manual weeding cum hoeing is done 45 days after planting, and the second one is carried out 120 days after planting.
- Bamboo/shrub staking is done 30–45 days after transplanting.
- Intercultural operations during second and third years may be carried out at least twice during each year.

Irrigation practices

- Irrigation may be provided as and when necessary.
- However, the plant may be grown as a rainfed crop in North-East India where the rainfall is high and evenly distributed throughout the year.
- Roots can be harvested after two years at preflowering stage in October or late fruiting stage by the end of November or even in early December when seed is required for next crop.
- The crop can, however, be allowed to stand in the field for three years.

Post-harvest management

- The hard roots are cut into small pieces and dried in the shade.
- The dried root pieces are packed in gunny bags for storage in cool and dry place.

Chemical constituents

- Roots contain resinous and extractive matter, gum, sugar, colouring matter, and salts of lime.
- The colouring matter consists of purpirin, manjistin, garancin, xanthine, besides several anthraquinone derivates[66-68].

Yield

- About 3 tonnes of dry root is obtained per hectare of cultivated crop.

3.0 AIM & OBJECTIVE

Internationally, over ten million new cases of cancer (all sites excluding nonmelanoma skin), with over six million deaths, were estimated. Since 1990 there has been a 22% increase in cancer incidence & mortality. Most frequent cancers were recording report indicated lung, breast, colorectal, and stomach. Although these figures are disquieting, some progress has been made in cancer diagnosis and treatment. Drug discovery from medicinal plants has played an important role in the treatment of cancer and, indeed, new clinical applications of plant secondary metabolites and their derivatives have been attempted towards combating cancer. Of all available anticancer drugs between 1940 and 2002, 40% were natural products or natural product-derived with another 8% considered natural product mimics.

And hence only in this present study anticancer activity of petroleum ether extracts of *Strobilanthes consanguineus* has been explored.

4.0 PLAN OF THE WORK

- Collection and authentication of the plants having antitumor activity.
- Extraction of dried plant materials in a Soxhlet apparatus using Petroleum ether .
- Preliminary phytochemical studies of extracts to identify phytoconstituents.
- MTT assay
- Ehrlich ascites carcinoma induced cancer in mice

5.0. MATERIALS AND METHODS

5.1 Plant collection and authentication

The leaves of strobilanthes consanguineus were collected from the local source, idukki,in the month of February. The plant material was identified and authenticated by prof P.Jayaraman Ph,D,director

Portions of plant material were collected and collected plants dried under sunlight. Make coarse powder with the help of mixer.

5.2 Animal Ethical Committee approval

Animal experiment was perfomed as per the protocol approved by the institutional animal ethical committee RVS COPS/IAEC/2019/006

5.3 Preparation of plant extract

Cold maceration technique was used for the extraction of plant material and a total of 200 g of *Strobilanthes consanguineus* leaves the coarse powder was used. During the process, 100 g of the coarse powder was soaked in an Erlenmeyer flask with 1 L of 50% of Petroleum ether and then placed on a shaker (Bibby Scientific Limited Stone Staffo Reshire, UK) tuned to 120 rpm with occasional shaking for 72 h at room temperature. The extract was filtered first using a muslin cloth and then Whatman grade No-1 filter paper and the marc was re-macerated for a second and third time by adding another fresh solvent. The filtrates were left overnight in a deep freezer and then lyophilized using freeze dryer. The dried plant extract was reconstituted with distilled water for oral administration.

5.4 Phytochemical Test

Chemical tests performed in the screening and identification of phytochemical constituents in the tested medicinal plants was carried out in extracts as well as powder specimens using the standard procedures.

5.4.1 Maeyer's reagent

0.355 g of mercuric chloride was dissolved in 60 ml of distilled water. 5.0g of potassium iodide was dissolved in 20 ml of distilled water. Both solutions were mixed and volume was raised to 100 ml with distilled water.

5.4.2 Dragendorff's reagent

Solution A: 1.7 g of basic bismuth nitrate and 20 g of tartaric acid were dissolved in 80 ml of distilled water. Solution B: 16 g of potassium iodide was dissolved in 40 ml of distilled water. Both solutions (A and B) were mixed in1:1 ratio.

5.4.3 Test for alkaloids

About 0.5 to 0.6 g of the methanolic plant extract was mixed in 8 ml of 1% HCl, warmed and filtered. 2 ml of the filtrate were treated separately with both reagents (Maeyer's and Dragendorff's).

5.4.4 Test for steroids

About 0.5 g of the methanolic extract fraction of each plant was mixed with 2 ml of acetic anhydride followed by 2 ml of sulphuric acid.

5.4.5 Test for terpenoids

An aliquot 0.5 ml of methanolic extract was mixed with 2 ml of CHCl3 in a test tube. 3 ml of concentrated H2SO4 was carefully added to the mixture to form a layer.

5.4.6 Test for flavonoids

To the substance in alcohol, a few magnesium turnings and few drops of concentrated Hydrochloric acid were added and boiled for five minutes.

5.4.7 Test for tannins

The 0.5 g of powdered sample of each medicinal plant leaves was boiled in 20 ml of distilled water in a test tube and then filtered. The filtration method used here was the normal.

5.4.8 Test for Phytosterol

The extract (2 mg) was dissolved in 2 ml of acetic anhydride, heated to boiling, cooled and then 1 ml of concentrated sulfuric acid was added along the side of the test tube.

5.4.9 Test for Phytosterol

1. Foam Test: 5 ml of the test solution taken in a test tube was shaken well for five minutes.

2. Olive oil test: - Added a few drops of olive oil to 2ml of the test solution and shaken well.

5.4.10 Test for glycosides

1.Keller -Killiani test: Added 0.4 ml of glacial acetic acid and a few drops of 5% ferric chloride solution to a little of dry extract. Further 0.5 ml of concentrated sulfuric acid was added along the side of the test tube carefully.

2. Hydroxyanthraquinone Test To 1 ml of the extract, added a few drops of 10% potassium hydroxide solution.

5.5 Experimental animals

The Adult female *S*wiss mice weighing between (20-30 g) were used to calculate LD_{50}. Both the sexes weighing between (180-200 g) were used for anti cancer activity. They were housed in clean polypropylene cages and maintained under standard conditions of light (12 hours with alternative day/night cycles), relative humidity (60-70%) and temperature (26 ± 1 °C). The animals were fed daily with rodent pellet diet and tap water *ad-libitum* under strict hygienic conditions.

5.6 Acute toxicity study

Experimental groups of mice was treated orally (p. o.) with aqueous extract of *Strobilanthes consanguineus* leaves at doses of (2000 mg/kg), control group of animals received normal saline by the same routes. Diazepam (2 mg/kg) was administered orally. All drugs were freshly prepared before each experiment. The doses of extracts were calculated to administer 1 ml of the suspension of extracts to the mice of 100 g. The procedure was followed as per OECD 423 guidelines (OECD/OCDE. 2002). The extract was administered orally at a dose of 2000 mg/kg body weight. Mice were kept under observed for 14 days to register possible mortality[69,70.]

5.7 MTT assay

The MTT assay, based on the conversion of the yellow tetrazolium salt-MTT, to purple-formazan crystals by metabolically active cells, provides a quantitative determination of viable cells. Cells will be plated on to 96 well plates at a cell density of 2×10^5 mL-1 per well in 100 µL of RPMI 1640 and allowed to grow in CO2 incubator for 24 h (37 ˚C, 5 % CO2). The medium will be removed and replaced by fresh medium containing different concentrations of sample for 48 h. The cells will incubated for 24-48 h (37 ˚C, 5 % CO2). Then, 20 µL MTT ([3- (4, 5-dimethylthiazol-yl)-2, 5- diphenyltetrazolium bromide]) stock solution (5 mg/mL in PBS) is added to each well and incubated for 5 h. The medium will removed and 200 µL DMSO is added to each well to dissolve the MTT metabolic product. Then the plate will shaken at 150 rpm for 5 min and the optical density is measured at 560nm. Untreated cells (basal) are used as a control of viability (100 %) and the results will expressed as % viability (log) relative to the control[71].

5.8 Ehrlich ascites induced cancer in mice

The mice can be divided into five groups comprising twelve animals in each group. The entire animal was injected with EAC cells ($2X10^6$ cells/mouse) intraperitoneally except for the normal group as follows: Group I: Normal (only sodium CMC Suspension (0.1%), Group II : Control (Induced EAC cell ($2\ X10^6$) with sodium CMC Suspension (0.1%) Group III : Standard (Induced EAC cell ($2\ X10^6$) with 5- fluorouracil 20mg/kg body weight) Group IV : (Induced EAC cell ($2X10^6$) with petroleum ether extract of *Strobilanthes consanguineus* low dose, Group V : (Induced EAC cell ($2X10^6$) with petroleum ether extract of *Strobilanthes consanguineus* high dose. All groups can be given with respective drugs 24 h after the tumor inoculation, once daily for 14 days. After the last dose and 24 h fasting, six mice in each group will sacrificed. The blood samples will be collected (14^{th} day) days)from the animals by retro-orbital puncher under slight anesthesia conditions and the hematological parameter such as red blood cells (RBC), white blood cells (WBC), differential count (DC), and hemoglobin (HB) were estimated by cell analyzer. The differential count of WBC carried out in the blood smear. The ascetic fluid is collected from the peritonSBC cavity of the animals, centrifuged and

divided into two parts. One part is centrifuged in a graduate centrifuge tube at 1,000 rpm for 10 min and the packed cell volume was measured. The cells in the other part of the ascetic fluid were separated by centrifugation and stained with trypan blue (0.4% in normal saline). The number of viable cells and non-viable cells was counted [71].The rest of the animals were kept to check average life span and change in body weight for six weeks.

6.0 RESULTS AND DISCUSSION

6.1 Appearance and percentage yield of Extract

Extracts were a semisolid brownish color extract and the percentage yield was found to be 10.35%w/v

6.2 Phyochemical Analysis

Below two observation indicated presence of Saponins Formation of stable foam confirmed the test & formation of a soluble emulsion confirmed the test. The formation of blue colour in acetic acid layer confirmed the test. Not formed red color in test tube absence of glycosides.

The phytochemical screening results revised that the after which it was observed whether the alkaloids were present by the indication of turbidity and/or precipitate formation. The colour changed from violet to blue or green in some samples indicated the presence of steroids. An interface with a reddish brown coloration was formed in the presence of terpenoids, as positive result. Red coloration identifies the presence of flavonoids (Shinado's test). A colour change was observed in the test tube, which indicated in the presence of tannins. A brown ring formation at the junction and the turning of the upper layer to dark green color confirmed the test for the presence of phytosterols

Table No. 1: Phytochemical Analysis

S.No	Phytochemicals	Inference
1	Alkaloids	+
2	Steroids	+
3	Terpenoids	+
4	Flavonoids	+
5	Tannins	+
6	Phytosterol	+
7	Saponin	+
8	Glycosides	-

+, Presence of the compound

- Absent

6.3. Acute toxicity

Plant a dose of 2000 mg/kg had no adverse effect on the behavioural responses of the tested mice up to 14 days of observation. Physical observations indicated no signs of changes in the skin, fur, eyes mucous membrane, behaviour patterns, tremors, salivation, and diarrhoea of the mice. There was no mortality observed and recorded weight loss is normal. Based on the above observation fix the doses 100, 200and 400 mg/kg for *in vivo* anti cancer activity

6.4 In Vitro Anti Cancer

In Vitro Anti Cancer Activity was performed by ether extract of *Strobilanthes consanguineus* . *Strobilanthes consanguineus* concentrations such as 18.5, 37.5 µg/ml, 75 µg/ml, 150 µg/ml & 300 µg/ml. Standard medication Cyclophosphamide antagonistic to tumor were performed among assorted concentrations such as 8.25, 16.25, 33, 66 & 100 µg/ml. The anticancer action of Pet ether extract of *Strobilanthes consanguineus* against HepG2 increased while in the centralization of Pet ether extract of *Strobilanthes consanguineus* IC50-(6.438±0.9057) exhibit great outcomes when compared amid standard cyp IC50-(34.52±0.9738). Beforehand, the anticancer movement of Pet ether extract of *Strobilanthes consanguineus has* been considered against SBCton's lymphoma ascite (DLA) cell lines, Human laryngSBC Hep-2 cell lines & human leukemic monocyte lymphoma individually.

Table No. 2: *In vitro* cytotoxic activity

Samples	Concentration (µg / ml)	% inhibition	IC50 (µ g / ml) Mean	SEM
		SBC	SBC	SBC
Pet ether extract of *Strobilanthes consanguineus*	19.65	2.25	64.39	0.9043
	38.40	53.82		
	76.00	65.44		
	150.0	81.27		
	300.0	92.53		
Standard Cyclophosmaide	8.15	22.45	35.52	0.9756
	16.15	34.23		
	33.00	56.78		
	66.00	69.39		
	100.00	78.56		

6.5 In Vivo Anti Cancer Activity

The rats body weight were expanded by assessment of tumor induced control group (17.98±0.35↑), Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC(7.68±0.35↑), CPG nano particles(200 mg/kg)+SBC (3.75±0.14↑) Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC(1.38±0.5↑) & CP drug (100 mg/kg)+ SBC(1.95±0.11↑) when contrasted amid Normal control(CMS susp) (20.48±0.51). Animals were amplified by assessment of tumor induced control group (0.23±0.05↑), Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC(0.17±0.03↑), Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC(0.9±0.9↑), Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC(0.1±0.05↑) when contrasted amid Normal control(CMS susp) (0.51±0.013) except

CP drug (100 mg/kg)+ SBC (0.2±0.0↓) treated groups were reduced compared to other groups.

The thymus gland weight investigation report showed that the body weight of all the groups of animals were increased by assessment of tumor induced control group (0.98=±0.4 Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC(0.6±0.1↑), Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC(0.5±0.04↑) Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC(0.1±0.05↑) & CP drug (100 mg/kg)+ SBC(0.00±0.05) when contrasted amid Normal control(CMS susp) (0.20±0.12).

The liver weight examination report showed that the body weight of all the groups of animals were increased by assessment of tumor induced control group (0.9±0.46↑), Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC(0.55±0.03↑), Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC(0.17±0.05↑), Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC(0.03±0.03↑) & CP drug (100 mg/kg)+ SBC(0.12±0.00↑) when contrasted amid Normal control(CMS susp) (2.86±0.16).

The kidney weight examination report demonstrated that the body weight of all the groups of animals were increased by assessment of tumor induced control group (0.39±0.01↑), Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC(0.26±0.03↑), Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC(0.23±0.02↑) Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC(0.15±0.02↑) & CP drug (100 mg/kg)+ SBC(0.11±0.1↑) when contrasted amid Normal control(CMS susp) (1.45±0.04).

The lungs weight investigation report demonstrated that the lung weight of all the groups of animals were increased by of tumor induced control group (0.11±0.03↑) & Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC(0.4±0.3↑) when contrasted amid Normal control(CMS susp) (0.67±0.03) & furthermore treatment groups of Pet

ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC(0.2±0.01↓) Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC(0.6±0.06↓) & CP drug (100 mg/kg)+ SBC(0.4±0.0.03↓) were diminished when contrasted amid of tumor induced control group (0.78±0.06), Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC(0.71±0.6) & to Normal control(CMS susp) (0.67±0.03).

Solid tumor volume examination report showed that the assessment of different day indication 15,20,25 & 30th variations of different groups of tumor volumes were decreased Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC(15th day 4.97±0.24↓), (20th day 0.6±0.13↓), (25th day 1.35±0.30↓) & (30th day 1.89±0.13↓), CPG Nan Ps (200 mg/kg)+SBC(15th day 4.39±0.22↓), (20th day 0.36±0.30↓), (25th day 1.21±0.36↓) & (30th day 1.75±0.13↓) Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC(15th day 3.78±0.24↓), (20th day 0.31±0.1↓), (25th day 1.46±0.11↓) & (30th day 1.80±0.13↓)& CP drug (100 mg/kg)+ SBC(15th day 3.63±0.13↓), (20th day 0.54±0.2↓), (25th day 1.47±0.23↓) & (30th day 1.79±0.3↓)when contrasted amid tumor induced control group (15th day 6.18±0.12↑), (20th day 0.98±0.6↑), (25th day 1.68±0.3↑) & (30th day 1.96±0.6↑).

Mean survival time test results showed that the survival time indication of all the groups of animals were improved by assessment of Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC (13.06±0.02↑) CPG Nan Ps(100 mg/kg)+ SBC (6.0±0.00↑), CPG Nan Ps(200 mg/kg)+SBC (9.12±0.38↑), Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC (14.13±0.47↑) when contrasted amid tumor induced control group (19.10±0.16),.

The life span examination have shown that all the groups of animals were increased by assessment of Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC (3.72%), CPG Nan Ps (200 mg/kg)+SBC(48.06↑), Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC(38.25%↑) when contrasted amid tumor induced control group (0.0±0.00↑),

The packed cell volume report showed that the all the groups of rats packed cell volume were constantly increased by assessment of Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg) + SBC (0.98±0.3↓), Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC (1.28±0.5↓) Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC (2.78±0.3↓) & CP drug (100 mg/kg)+ SBC (2.66±0.03↓) when compared amid assessment of tumor induced control group (4.84±0.13).

Viable cell counts report indicated that the all the groups Viable cell counts were constantly increased by assessment of Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC (5.98±0.00↓), Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC (8.00±0.76↓) Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC (11.38±0.16↓) & CP drug (100 mg/kg)+ SBC (11.18±0.00↓) when contrasted to tumor induced control group (14.54±0.16).

The non viable tumor cell count results revealed that the all the groups of animals were increased by assessment of Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC (0.97±0.02↑), Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC (2.1±0.08↑), Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC (0.53±0.020↑) compared to tumor induced control group (1.7±0.2↓).

The hematological parameters were altogether ($P < 0.001$) adjusted following 15 days of treatment when contrasted & the SBC control aggregate. The aggregate WBC counts have been increased the SBC control cell while, the RBC count, hemoglobin levels & WBC diminished the SBC control cell. In the wake of treating for 15 days treatment of different doses of Pet ether extract of *Strobilanthes consanguineus* such as 100, 200 & 400 mg/kg, the body weight & hematological parameters had standardized, near the ordinary gathering. The WBC fundamentally diminished in all the groups Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC (2.55±0.41↓), Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+SBC (2.84±0.0↓) Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC (4.02±0.41↓) & CP drug (100

mg/kg)+ SBC (3.73±0.14↓) when contrasted to tumor induced control group (12.86±0.13).

The RBC counts ($P < 0.01$) were constantly increased in the form of Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC (1.6±0.39↑), (100 mg/kg)+ SBC (0.83±0.41↑), (200 mg/kg)+SBC (1.06±0.35↑), Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC (1.91±0.20↑) when contrasted amid tumor induced control group (3.06±0.54). Additionally, hemoglobin fundamentally ($P < 0.001$) increased Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC (3.79±0.30↑), Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC (1.32±0.1↑), (200 mg/kg)+SBC (2.14±0.32↑) & Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC (4.1±0.28↑) when contrasted with tumor induced control group (9.84±0.56).

Table No. 3: Effect of CPG extract on relative organ weights of normal control, tumor induced (SBC) & drug treated mice

Treatment	Relative Organ Weight (g/100g body wt.)					
	Body weight (g)	**Spleen**	**Thymus**	**Liver**	**Kidney**	**Lungs**
Normal control	21.48±0.58	0.52±0.26	0.21±0.012	2.87±0.16	1.43±0.04	0.69±0.03
Tumor induced control	39.52±0.016	0.64±0.018	0.22±0.016	3.78±0.62	1.55±0.05	0.79±0.06
Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC	28.16±0.16	0.68±0.016	0.26±0.011	3.41±0.6	1.71±0.07	0.71±0.06
Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+ SBC	24.23±0.37	0.61±0.04	0.23±0.08	3.13±0.11	1.65±0.02	0.65±0.02
Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC	21.86±0.56	0.53±0.08	0.27±0.07	2.82±0.19	1.62±0.02	0.67±0.09
Standard drug (100 mg/kg)+ SBC	25.43±0.62	0.46±0.06	0.21±0.017	2.90±0.016	1.52±0.05	0.60±0.06

Figure No. 7 : Effect of CPG extract on relative organ weights

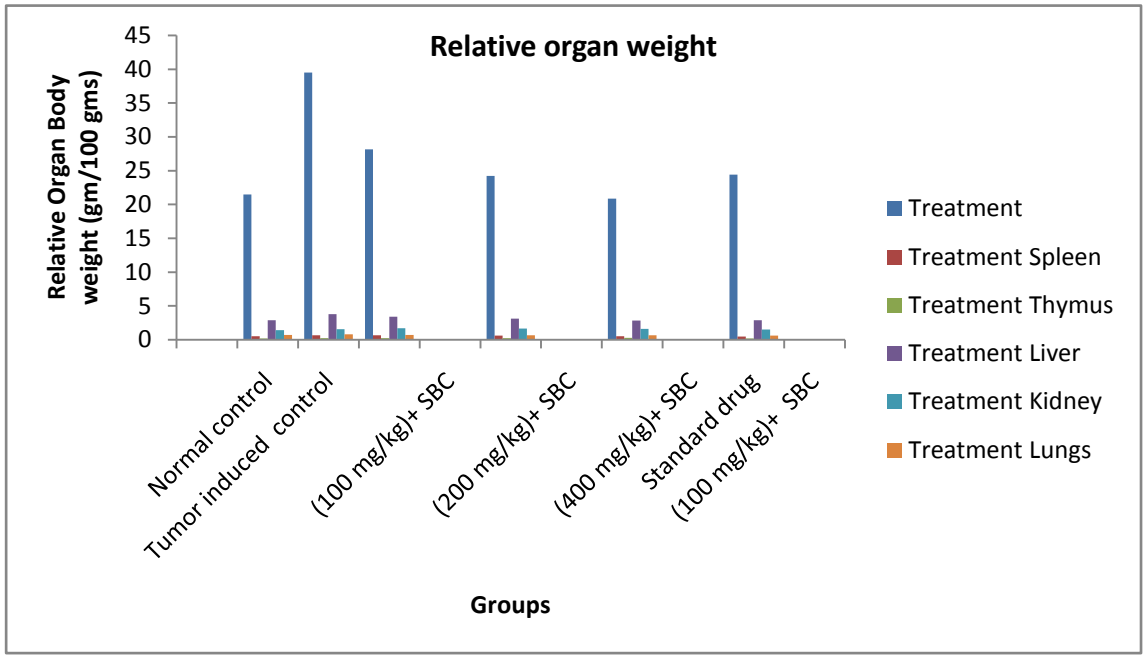


Table No. 4: Anticancer activity of CPG extract on solid tumor volume in tumor (SBC) induced mice

Treatment Groups	Solid Tumor Volume			
	15th day	**20th day**	**25th day**	**30th day**
Tumor induced control (CMS susp)	6.28±0.12	8.29±0.18	7.86±0.15	8.14±0.16
Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC	4.97±0.24	4.71±0.11	3.82±0.54	3.08±0.11
Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+ SBC	4.39±0.22	4.03±0.52	3.18±0.82	2.64±0.11
Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC	3.71 ±0.24	3.47±0.23	2.30±0.6	1.90±0.11
Standard drug (100 mg/kg)+ SBC	3.72±0.6	3.19±0.15	2.16±0.36	1.85±0.16

Table No. 5: Observed parameters of survival time, life span, tumor volume, viable & non-viable cell count

Treatment	Mean Survival time (Days)	Increase of life span (%)	Packed cell volume	Viable cell count X 10^6 cells/ml	Non-viable tumor cells count X 10^6cells/ ml
Tumor induced control	19.10±0.16	-	4.84±0.6	14.54±0.16	1.84±0.06
Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC	25.16±0.16	35.72	3.86±0.16	8.56±0.16	2.81±0.011
Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+ SBC	28.28±0.54	48.06	3.56±0.18	6.54±0.92	3.94±0.021
Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC	33.23±0.63	73.97	2.06±0.16	3.16±0.52	2.37±0.033
Standard drug (100 mg/kg)+ SBC	32.16±0.18	68.37	2.18±0.16	3.36±0.16	3.54±0.015

Table No. 6: Observation of hematological parameters in tumor bearing mice

Parameter	Hb (gm %)	RBC (million/mm^3)	WBC (10^3 cells/ mm^3)
Normal control	14.12±0.26	5.54±0.26	8.65±0.15
Tumor induced control	9.12±0.56	3.06±0.54	11.86±0.6
Pet ether extract of *Strobilanthes consanguineus* (100 mg/kg)+ SBC	12.16±0.55	3.85±0.6	11.31±0.54
Pet ether extract of *Strobilanthes consanguineus* (200 mg/kg)+ SBC	11.94±0.24	4.10±0.19	10.00±0.6
Pet ether extract of *Strobilanthes consanguineus* (400 mg/kg)+ SBC	6.96±0.84	4.55±0.34	8.92±0.54
Standard drug (100 mg/kg)+ SBC	6.37±0.86	4.72±0.15	9.8±0.27

Figure No. 8: Anticancer activity of CPG extract on solid tumor volume

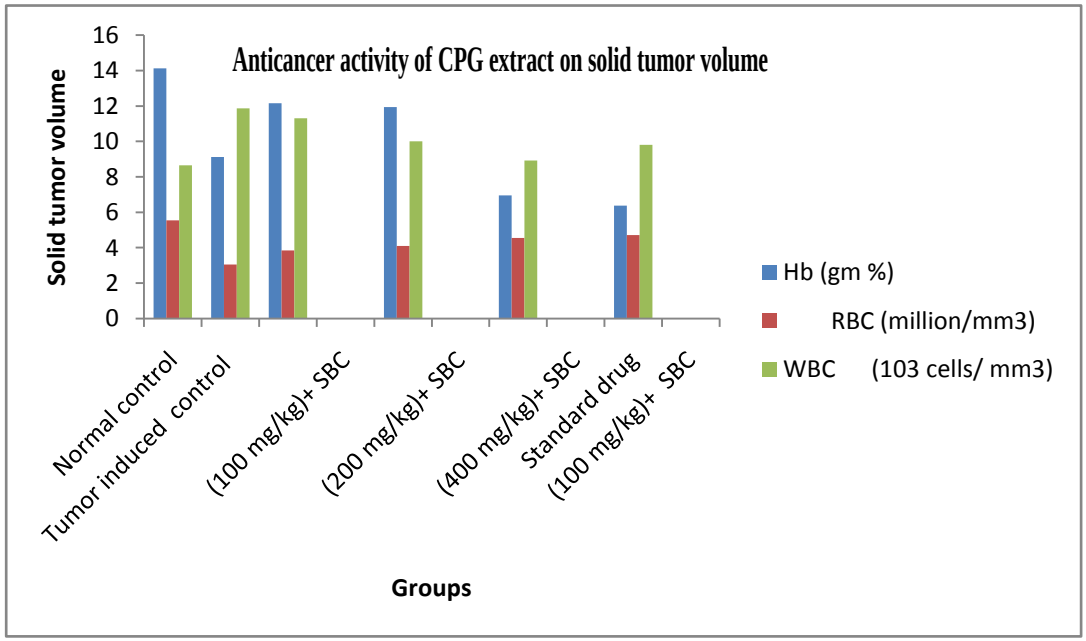
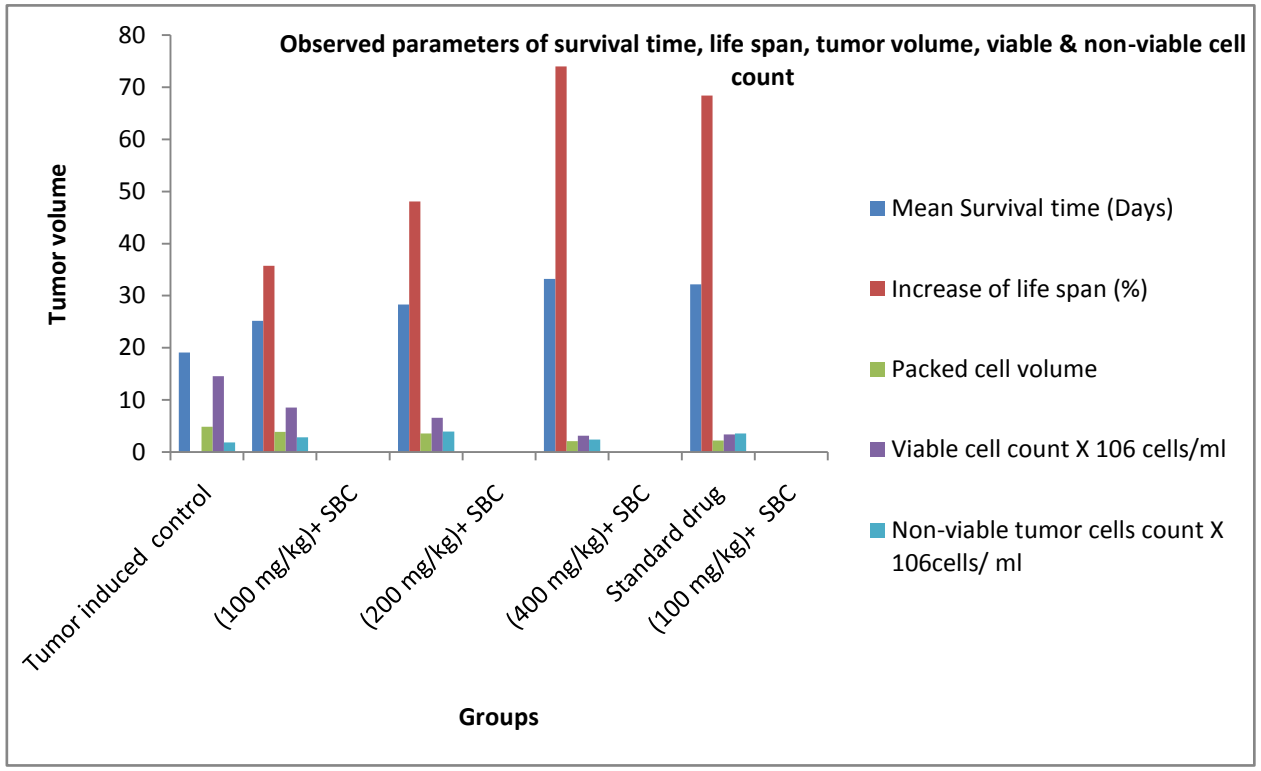


Figure No 9: Observed parameters of survival time, life span, tumor volume, viable & non-viable cell count



7.0 CONCLUSION

Essential significance will be upgrade the pharmacokinetics & pharmacodynamics as for extract the most part the previously mentioned characters are less, despite the fact that it has got extraordinary anticancer activity. India is one of the most promising regions for discovering novel Biologically-active substances from its flora. More efforts are needed to explore potent anticancer plants from the mother earth and save humans around the world from cancer. Extensive research will be needed to determine the individual component responsible for the anticancer. By embracing the reasonable techniques to defeat the solvency issue of the *Strobilanthes consanguineus* is the real reason for concern.

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